ON THE

NATURE AND TREATMENT

OF

DIABETES.

RESEARCHES

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OF

DIABETES.

BY

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PREFACE.

It is now about six years since the first edition of this work appeared, and for upwards of two years it has been out of print.

In the preparation of the present volume the book has been re-modelled and, in great part, re-written. Much new matter has also been added. It may be said, indeed, to form a new work, and no pains have been spared in carrying out the endeavour to render it more worthy the favorable reception that was accorded to its predecessor. Availing himself also of the experience that has been thrown in his way through the medium of the first publication, the author hopes that his efforts to produce a more useful treatise upon diabetes to the medical practitioner have not been fruitlessly exerted.

The views introduced into the first edition upon the subject of glycogenesis have been confirmed by the author's subsequent experience, and also by the experimental results obtained by other physiologists, both at home and abroad, as will be seen from what is contained in the present work. By the German translation that was published at Göttingen, in 1864, unknown to the author until after its appearance, a full ventilation of his views has been afforded on the Continent.

35, GROSVENOR STREET,
GROSVENOR SQUARE.

December, 1868.

ON THE DETECTION

AND

QUANTITATIVE DETERMINATION OF SUGAR.*

Diabetes mellitus is a disease which calls for the application of chemistry for the purpose of diagnosis. It is true the experienced physician may, from the history, symptoms, and appearance of the patient in a well-marked case, pretty safely surmise the existence of the disease, but to be enabled to speak in a positive manner an examination of the urine is required. The examination should be directed in the first instance towards ascertaining whether sugar exist or not; and in the next place, in the event of sugar being found, to the determination of its amount. To ascertain simply that sugar is present in the urine is, it must be said, to obtain but very meagre information about a case. What is also wanted before anything definite can be said is a knowledge of the amount of sugar that is being passed, and the effect of treatment can only be with precision watched by a quantitative examination of the urine, conducted from time to time.

* Messrs. Griffin and Sons, of 22, Garrick Street, Covent Garden, supply the apparatus referred to in the following pages upon the subject of analysis.

Of the varieties of sugar that chemists enumerate, glucose or grape sugar is that which the pathologist has to deal with. There are various means by which its presence may be displayed, but only those in common use need be referred to here. Fortunately for the prosecution of physiological and pathological researches bearing upon sugar, it happens that this principle is one of the most easily recognisable of organic bodies. It may be said, indeed, to be susceptible of detection with almost the same facility and certainty as an inorganic substance, and this, when present, even in very minute quantity.

QUALITY OF SWEETNESS.

Sweetness is one of the most striking properties possessed by sugar, but it is not characteristic of it, and our sense of taste, although sometimes appealed to, is not one that it is convenient and agreeable, nor even at all times safe, to employ to supply information in investigations of an analytical kind. Still, by the sweet taste of their urine diabetic patients have before now themselves discovered the nature of their complaint, and the property of sweetness possessed by diabetic urine was recognised and dilated on by medical authorities before anything was known about the present mode of testing for sugar. Dr. Willis, it seems, was the first to point out the character of sweetness belonging to the urine in diabetes. "The subjects of this affection," said Willis, "pass more urine than the whole quantity of fluids taken into the body; they have besides a constant thirst and a slow kind of hectic fever always on them. It is very far from true, as some authors affirm, of the drink being again discharged with little or no alteration, for the urine in all that I have seen (and I believe it will universally be the case) differed, not only from their drink, and from every other fluid in the animal body, but was like as if it had been mixed with honey or with sugar, and had a wonderfully sweet taste."

The property of sweetness is not a character that it is necessary to recommend in our day to be looked for by the medical practitioner in order to discover if sugar be present in the urine; indeed, if the recommendation were made, it is not probable that it would often be carried out. There are several ways now known by which the point may be otherwise determined.

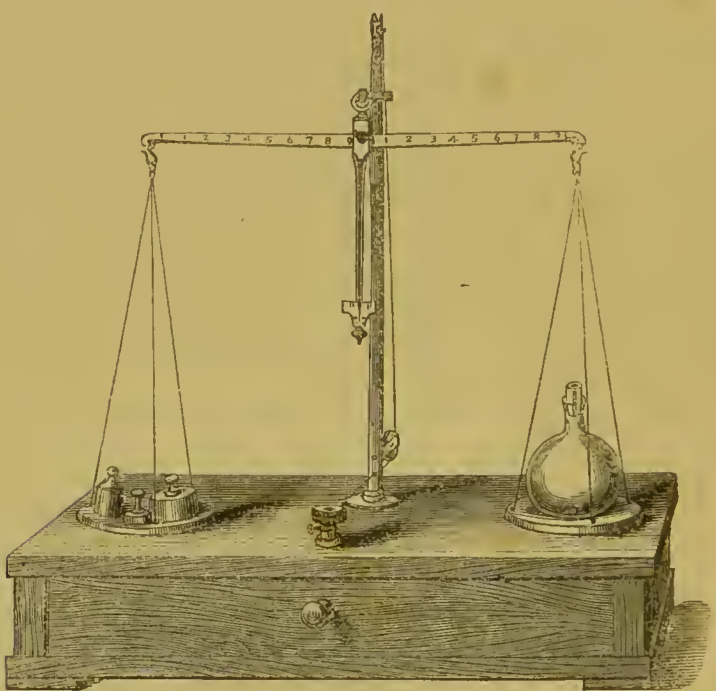
SPECIFIC GRAVITY.

From the specific gravity of the urine a rough conclusion can be drawn as to the existence of diabetes or not, but it should not be relied upon solely. The sp. gr. simply indicates the amount of solid matter that is contained in the urine. Where diabetes mellitus exists sugar is added to the solid matter naturally present, and so the sp. gr. is raised beyond its natural range. Should only a moderate quantity of sugar be present the sp. gr. would not supply much information, because the proportion of solid matter naturally belonging to the urine is subject under different circumstances to considerable variation; but should the sp. gr. be uniformly maintained at a height much beyond its natural limit, and the quantity of urine be at the same time excessive, diabetes may be presumed with pretty fair certainty to exist.

To determine the sp. gr., either *weighing* or the use of an instrument known as the *hydrometer* (*urinometer* this instrument is called, as specially graduated for the examination of urine), or of little *bulbs* or *beads* such as are figured at p. 8, may be employed.

Weighing supplies the most precise information, and should be resorted to for taking the sp. gr. of a fluid in all cases where minute accuracy is required. The sp. gr. bottle is used for the purpose. This consists of a thin glass flask (shown in fig. 1), provided with

FIG. 1.



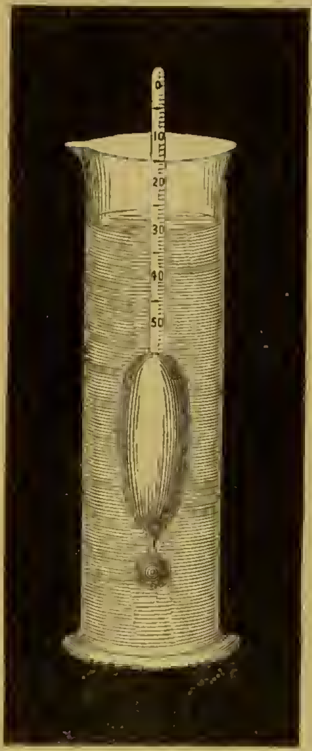
Balance with sp. gr. bottle for determining the sp. gr. by weighing.

a perforated glass stopper. Bottles are sold holding, when full, 1000 and 500 grains of distilled water. When filled with a heavier liquid and placed in the balance, the weight will, of course, be more. The counterpoise of the flask must be placed in the opposite scale with the weights. Suppose, for illustration, the 1000-grain bottle to be used, and to have been filled with urine. The glass stopper of the bottle being perforated, allows it to be filled without including any air-bubbles. Urine having been poured in completely to the top, the stopper is applied and will be permitted to sink into its proper place by the displacement of fluid through its perforated centre. The bottle is then wiped dry upon its exterior, and placed in the balance with the counterpoise in the opposite scale. The weight observed, let it be say 1040 grains, represents the sp. gr. If a flask holding 500 grains of distilled water has been used, the weight observed requires to be doubled to get the figures in the way they are given.

In the ordinary examination of the urine such minute precision is not required as to necessitate the use of the balance; and it is rarely employed, as the plan about to be spoken of affords a much quicker means of arriving at the information required.

The *hydrometer* or *urinometer* is an instrument the form of which is shown at fig. 2. It is to be procured in both glass and metal, but on the score of greater cheapness, and there is a considerable difference in the price of the two, glass ones are most commonly used. Its operation depends upon the principle that bodies floating in a liquid displace a bulk equal in weight to themselves. The lower bulb is weighted so as to cause the instrument to sink nearly to the top of the limb when placed in distilled water. In a heavier liquid it does not sink so far—so much of the limb, in other words, is not immersed, or so much fluid displaced. The descent of the instrument thus varies according to the density of the liquid in which it is immersed, and the limb is provided with a scale representing the various degrees within the range that is likely to be encountered.

Fig. 2.



Urinometer.

All that is necessary in using the urinometer is to immerse the instrument into the specimen of urine to be examined, and when it is floating steadily to note the degree on the scale that is on a line with the surface of the liquid. This denotes the sp. gr. of the urine. Should the degree, for instance, be 25, the sp. gr. will be read off as 1025. On account of the limited space at disposal in the limb, the last two figures only are introduced on the scale.

With a correctly registering instrument, the indications of the urinometer may be looked upon as quite accurate and precise enough for all ordinary purposes. It must unfortunately be said, however, that it is rare to meet with an instrument that is correct throughout its entire register, and many are to be come across that are even several degrees out in some part or other of their scale. This arises from the low price at which they are got up for sale, not allowing proper time to be given to secure a correct graduation. The usual plan adopted is to mark only the two extreme points from observation, and to separate the intervening space into regular divisions. Any inequality in the calibre of the limb, and it is scarcely likely to be true throughout, will necessarily lead to a faulty graduation in proportion to its extent.

It has often come across me to hear of instruments unpardonably incorrect, and I have several times known serious mistakes committed by reliance having been placed upon the indications they have afforded. As an instance in point, a medical practitioner from the country, on consulting me about himself, mentioned that some time previously he had been led to suspect that he was suffering from diabetes, from having experienced some of the characteristic symptoms of the complaint, but concluded that his suspicions were unfounded upon examining his urine with the urinometer in his possession, and finding that the sp. gr. indicated was not outside the natural range. His symptoms increasing, he was afterwards induced to get his urine examined by a neighbouring medical man, and then it was discovered that he really was labouring under the disease. His own urinometer, he told me, had indicated a sp. gr. not very much over 1020, when the actual sp. gr. of his urine was about 1040. He had gone on for about two months before he discovered that he had been thus misled.

I have known also examples of a converse kind to occur. Diabetes has been assumed to exist, and the patient has been placed and kept for some time upon the dietetic treatment for the disease before the error has been discovered.

It is much to be deplored that the urinometers sold are so little to be depended upon for accuracy as they are, but at the same time no one should rely in a matter of diagnosis upon the sp. gr. alone of the urine. Where a suspicion of diabetes exists the urine should always be subjected to a chemical examination before any decision is arrived at. Even with a correctly registering instrument mistakes might sometimes be made by relying too much upon the sp. gr. I may mention a case bearing upon this point, which, at the time it fell under my observation, made a strong impression upon me. A gentleman was brought to me by a medical practitioner for my opinion regarding the state of his urine. He had been rapidly losing flesh and presented a very emaciated appearance, just such an appearance as led me to suspect that he was suffering from diabetes. He had also thirst, and according to his own account was passing an excessive quantity of urine. On first looking to the sp. gr. of the urine, a specimen having been passed for examination during his interview with me, I found it to stand at 1036. My suspicions were thus strongly supported, but it turned out, on applying a chemical test, that no trace of sugar was to be discovered. In reality, no diabetes existed.

The sp. gr. *bulbs* or *beads* furnish another means for ascertaining the density of a liquid. They are made of glass, and present the form shown in the accompanying sketch. Each bead serves only for indicating the particular density which it has engraved upon it. When plunged into a liquid of this density it neither sinks to the bottom nor floats upon the top, but swims at any height that it may chance to settle. For raising or lowering the density

FIG. 3.

Sp. gr. bulb.

of a fluid to a given point these bulbs are admirably adapted, but for indicating the density that exists they are not very convenient, as beads of different densities require to be tried until the one is found which neither sinks nor floats.

LIQUOR POTASSÆ TEST.

This is also commonly known as *Moore's test*, from the name of its proposer. It is founded on the decomposition that grape sugar undergoes at a boiling temperature in contact with an alkali. Glucic acid is first formed, and afterwards converted into melassic acid, the solution of which presents a dark brown, or in a concentrated form a black, colour.

For the application of the test, let about a drachm or a couple of drachms of the suspected urine be placed in a test tube, and be treated with about half its bulk of liquor potassæ. Heat is then to be applied by means of a spirit lamp, and should sugar be present the contents of the tube will soon acquire a brownish colour, which is found to become more intense as the boiling is continued. Where the quantity of sugar is not large the tint assumed is somewhat similar to that of dark-coloured sherry, but when large the colour is very much deeper.

For the detection of diabetes this test will answer the purpose, but it is not one that is adapted for the prosecution of physiological research. Where small quantities of sugar are being dealt with, something giving a more decided indication than that afforded by a slight difference of shade in colour constitutes what is needed.

The indication of the liquor potassæ test, it must be borne in mind, is open to a serious fallacy when the liquor potassæ happens to be contaminated with lead, which is not unfrequently the case. Flint glass contains a large quantity of lead, and an alkaline solution on being kept in a bottle of this description dissolves out, and thus becomes contaminated with, some of the metal. Lead may also find its way into the test from the glaze of an earthenware capsule in which the potash during its preparation may have been evaporated down. No matter what the source whence the lead has been derived, it is found, on boiling liquor potassæ contaminated with it with organic matter containing sulphur, that the sulphur and the lead combine and produce a dark-coloured compound. Thus an effect closely resembling the reaction produced by sugar may be obtained and the conclusion be drawn, by those unaware of what has been mentioned, that sugar is present where none in reality exists. If the liquor potassæ test be made use of, it is necessary to guard against exposure to error by first ascertaining that the liquid employed is in a proper state of purity. To maintain it in this state, it must afterwards be kept in a bottle devoid of lead, and one of green glass will furnish what is wanted.

The liquor potassæ test is not a test that I often employ, because I believe that in the different forms of copper solution about to be spoken of we have much more trustworthy and delicate—and therefore better—reagents.

COPPER TESTS.

Grape sugar is endowed with the power of exerting a de-oxidizing action upon several metallic solutions. The oxides contained in them are reduced by its influence either to a lower state of oxidation or, it may be, to the metallic state altogether. This property is sufficiently characteristic of sugar amongst organic bodies to render such metallic solutions valuable agents as tests for its detection. They are also available for effecting its quantitative determination. Solutions of copper, mercury, silver, gold, and platinum, are amongst those that are acted upon by sugar. Copper, however, is the metal the preparations of which may be considered to be the best adapted for the purposes of a test, and it is to these only that I consider it necessary here to refer.

There are various forms of copper test in use, but in all of them the principle of action is the same. The oxide of copper, which must exist in the test in a free state, is reduced in contact with grape sugar at a boiling temperature to the condition of suboxide. It gives up half its oxygen, and falls as a yellow, orange-yellow, orange-red, or brownish-red precipitate, according, apparently, to the state of hydration: at all events, where only a small quantity of sugar exists in the liquid examined, the precipitate presents more or less of a yellow colour; whilst when a large quantity is present, the colour observed is orange-red or even reddish-brown.

It is only with grape sugar, and not cane, that the copper test reacts. If it be wished to look for cane sugar it is easy by boiling with a little sulphuric acid to convert it into grape sugar, and then its presence, by the subsequent reaction of the copper test, applied after the sulphuric acid employed has been neutralized, may be displayed.

Trommer's test.—This constitutes one of the varieties of copper test. The oxide of copper is set free at the time of application, which is conducted as follows. A drop or a couple of drops of a solution of sulphate of copper of moderate strength are let fall into about a drachm of the specimen of liquid to be examined, contained in a test tube. Liquor potassæ is then added in excess. A blue precipitate, consisting of the hydrated oxide of copper, is produced on the first addition of the alkali; but this, should sugar be present, becomes redissolved on adding a larger quantity, giving rise to a deep blue-coloured liquid in the place of the faint blue that had been produced by the sulphate of copper alone. Where no sugar is present the precipitated oxide of copper is not redissolved by the alkali added in excess. It is not this, however, that is relied upon to decide as to the presence or absence of sugar. On boiling the contents of the test tube the presence of sugar leads to the production of a copious orange-coloured deposit of suboxide, whereas under its absence no change is produced.

Trommer's is not, I consider, the best copper test to select. It is less quick and ready of application than the form of test where the oxide of copper is contained in solution, as in the liquids about to be referred to. It is also not so delicate in its indication as the solutions, for where only traces of sugar exist they may escape recognition by the small amount of reduced oxide produced being obscured by the undissolved prot-oxide that is diffused around.

Copper test solutions.—When an alkali is added to a solution of sulphate of copper a bulky precipitate, consisting of the hydrated protoxide of copper, is thrown down. No excess of the alkali redissolves this precipitate when the alkali and the salt are alone brought together. Should some kind of organic matter, however, happen to be present, then the precipitated oxide is found to be dissolved by the alkali added in excess. Thus, the oxide of copper in a pure state is not soluble in an alkali; whilst, in contact with organic matter free solubility, on the other hand, is the result. Hence the reason in the employment of Trommer's test that, under the presence of sugar, the precipitated oxide disappears and a clear blue liquid is produced on the addition of the liquor potassæ in excess.

With the aid of organic matter, then, a liquid is procurable in which free oxide of copper is held in solution. The organic matter selected for use must necessarily not have the power of effecting a reduction of the oxide at the temperature of boiling, otherwise the test by itself would give a reaction. Tartaric acid is of the kind required, and constitutes the agent that is ordinarily employed.

There are various forms of copper solution employed as tests for sugar. They all, however, it may be said, essentially consist of oxide of copper held in solution by an alkali through the medium of organic matter which, unlike sugar, has not the property of exerting a de-oxidising influence at the temperature of ebullition. Barreswil's liquid, which constitutes a much used form of sugar test on the Continent, is made with sulphate of copper, bitartrate of potash (cream of tartar), carbonate of soda, potash, and water. The carbonate of soda is introduced to neutralize the excess of acid in the bitartrate of potash. By taking at once the neutral tartrate instead of the bitartrate of potash the call for the use of the carbonate of soda is dispensed with ; and it appears to me better, on account of being more simple, to prepare the test in this way. Fehling's solution, which is made with sulphate of copper, tartrate of potash, and caustic soda, forms a liquid of this kind. The solution I have been for many years in the habit of employing myself is a modification of Fehling's, caustic potash being substituted for the caustic soda.

The following are the ingredients of which it is composed:

Cupro-potassic test solution for Sugar.

Sulphate of copper	320 grains.
Tartrate of potash (neutral) . .	640 ,,
Caustic potash (*potassa fusa*) . .	1280 ,,
Distilled water	20 fluid ounces.

In making the solution the sulphate of copper is dissolved separately in ten ounces of the water, and the tartrate of potash and potash together in the remainder. The solution of sulphate of copper is then poured into that of tartrate of potash and potash. In this way no precipitate is produced, as happens should the mode of mixing be reversed. The liquid obtained is clear and bright, and of a beautifully deep blue colour. It is capable of being employed, as will be seen further on, for estimating the amount as well as for detecting the presence of sugar. For employment as a quantitative test, the greatest exactitude is, of course, required in its preparation.

A test liquid may be conveniently prepared, where a small quantity only is required, by pounding together five grains of sulphate of copper and ten grains of tartrate (neutral) of potash, and dissolving in two drachms of liquor potassæ. A clear deep blue liquid is formed, which answers quite as well for the detection of sugar as any other form of copper solution.

It is necessary to be aware of the fact that all the copper solutions are liable, after having been kept for some time, and especially when kept exposed to the light, to allow a slight reduction to occur on full boiling without any sugar being present. Some change must evidently have taken place in the fluid itself. Probably the amount of free alkali has been diminished by being converted into a carbonate, for the addition of free alkali restores the liquid to a proper state. It is only a slight deposit that occurs from this circumstance, one that could not be mistaken for the reaction of strictly diabetic urine, although it might lead to the inference that a trace of sugar existed. The state of the test can very easily be ascertained by boiling a little of it in a test tube alone. As a matter of precaution, this, after the fluid has been made beyond a few weeks, should be occasionally done, in order to see that it is in a proper state. Should any change be noticed on its being boiled, the addition of a fragment of caustic potash will render it as fit as ever again for use.

Sugar is not quite the only organic principle by which the copper test is reduced. Its reaction, therefore, cannot be taken as affording an absolutely positive indication that sugar is present. It is stated that glycerine, tannine, cellulose, leucine, uric acid, and chloroform, are capable of exerting more or less reducing action upon it. Chloroform certainly produces a strong effect. Uric acid I have found occasion a slight deposit of suboxide. Cotton (cellulose) I have also seen give rise to just a trace of precipitate, but with glycerine I have not noticed that any reaction whatever has occurred. Glycerine, indeed, has appeared to me to be an agent that might be not inappropriately used to take the place of the tartrate of potash in the preparation of the solution.

Although from what has just been said the reaction of the copper test is not to be looked upon as affording unequivocal evidence of the presence of sugar, still in actual practice it is found to be one of much value, and one with a little precaution that is scarcely likely to mislead. Indeed, certainly where small quantities of sugar are in question, my experience would incline me to place more reliance upon the behaviour of the copper test than on that of any other. There is no test, it must be said, that can be spoken of as affording an absolutely indisputable indication, for even the fermentation test, as will be seen further on, has its fallacies as well as the others.

Another circumstance that it is necessary to be aware of in the employment of the copper tests is the fact that under certain conditions there may be no fall of suboxide, notwithstanding that sugar may be indisputably present. Ammoniacal salts have the property of occasioning this result. Ammonia and its salts, it is found, possess a solvent power over the suboxide of copper, and hence when they happen to be present no precipitate is produced by the action of sugar. The combined ammonia contained in urine is often sufficient to obscure at first the presence of sugar when the quantity does not happen to be large. I have often noticed on examining urine—I do not mean diabetic urine, for this, unless albumen be present, always gives a neat reaction at once—that no change has at first resulted, whilst after boiling for some little time a copious amount of suboxide has fallen. Ammonia has been recognised escaping from the test tube, the potash contained in the test liquid having set it free for it to be driven off by the heat employed. After a little boiling the test has changed to a yellow or brownish-yellow colour, but without any deposit being produced, there being still sufficient ammonia present to hold the suboxide in solution. By further boiling the remaining ammonia has been expelled, and then the precipitate has appeared.

The presence of albuminous matter also interferes with the reaction of the copper test; and it is probably to the generation of ammonia, as a product of decomposition produced by the influence of the alkali contained in the test, that the effect is attributable. I have known the existence of albumen conceal the presence of sugar in urine where even a considerable quantity has existed. Should a negative result be obtained on testing a liquid containing albumen, the albumen must be separated and the liquid again examined before it can be pronounced to be free from sugar.

In the case of urine the separation of albumen may be effected with the greatest facility, all that is required being to submit the specimen to boiling and filtration. With blood, however, and other animal products, it does not happen that all the albumen can be got rid of so easily. Unless, however, it has been entirely separated no reliance can be placed upon the result.

To prepare a specimen of blood for testing, one of the following processes may be adopted.

It is on account of its alkalinity that boiling does not suffice to precipitate all the albuminous matter from blood and leave a suitable liquid for testing. By neutralizing its alkalinity and then boiling, a clear and colourless liquid is obtained on filtration. For this purpose acetic acid may be cautiously added until the exact point of neutralization is obtained. Care is required not to exceed the point, for an excess, even a slight excess, of the acid operates in the same way as the original alkalinity. Being a solvent of albuminous matter, the presence of acetic acid in a free state gives rise to a condition identical in effect with that which its employment was intended to remove. On account of this circumstance the neutralization process is found a little troublesome in practice.

A more easily applied process is one which consists in boiling the blood with sulphate of soda. A small quantity, say about half an ounce, of blood is placed in a small porcelain capsule, and treated with about its own bulk of crystallized sulphate of soda reduced to small fragments or to a powder. Heat being then applied, and the contents of the capsule briskly boiled, it will be found that a perfectly limpid colourless liquid is readily obtainable by filtration. The sulphate of soda, with the employment of heat, causes the precipitation of all the albuminous and colouring matters, and the only circumstance to attend to is that enough is used to secure that this is completely effected. The presence of sulphate of soda in the filtered liquid in no way interferes with the subsequent application of the copper test.

The use of animal charcoal has also been recommended for preparing a specimen of blood for testing. It is well known to enjoy an extensive absorbent power; but, according to Bernard, glucose forms a principle that it does not take up. Hence by its means, according to the same authority, albumen and colouring matter may be removed from blood; albumen and uric acid, from urine; and caseine and fatty matter, from milk; leaving whatever sugar may be present to pass through the filter and be contained in the filtrate. I have several times tried this process, but my experience does not lead me to recommend it for use.

For examining a solid material, such as the substance of the liver, &c., a suitable liquid may be obtained for testing, either by making a plain decoction of it; or else, by pounding it in a mortar with nearly an equal bulk of sulphate of soda, and then heating and filtering in the same manner as was recommended for blood.

The copper test is a very delicate one, and will display the presence of minute quantities of sugar in urine without any preliminary preparation. Where, however, an exceedingly minute quantity is being looked for the urine may be concentrated by evaporation, and treated with an excess of acetate of lead to get rid of colouring and other solid matters in the form of precipitate. The lead contained in the filtrate, belonging to the excess of acetate employed, is best removed by a stream of sulphuretted hydrogen. After a second filtration the copper test may be applied.

The 'Quarterly Journal of the Chemical Society,' April, 1861, contains an analysis by Dr. Bence Jones of the relative merits of different processes for the detection of minute quantities of sugar in the urine. By means of one of the processes recommended by Brücke the seventh part of a grain of grape sugar dissolved in about seven fluid ounces of urine was not only to be detected, but two thirds of it were recovered. The urine was treated first with the neutral and then the basic acetate of lead. The precipitate was separated by filtration, and ammonia added to the filtrate. In the precipitate now produced the chief part of the sugar was contained. The next step consisted in treating this precipitate with a solution of oxalic acid, or suspending it in water and subjecting it to the influence of a stream of sulphuretted hydrogen. Filtration was again performed, and the filtrate contained the sugar in a suitable state for recognition.

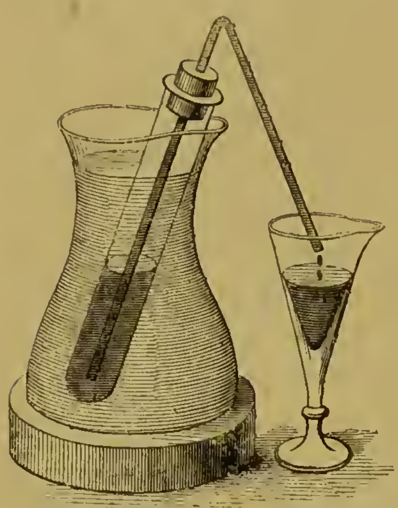
FERMENTATION TEST.

It is a well-known property of sugar, the one it enjoys of undergoing conversion into alcohol and carbonic acid—fermentation, as it is called—when brought in contact with yeast and exposed to moderate warmth. Both grape and cane sugar are susceptible of this change, but the former is found to be more freely so than the latter. Indeed, it is thought that cane sugar has to be converted by the ferment into grape sugar before it undergoes fermentation. The agent endowed with the power of producing this change consists of living cells constituting a low form of vegetable growth which has received the name of *Torula cerevisiæ*. Through the influence of the changes attendant upon the growth of these cells, an alteration in the grouping of the elements of grape sugar ensues: in other words, a re-arrangement, unattended with either loss or gain, takes place, which results in the production of alcohol and carbonic acid.

The property of undergoing the alcoholic fermentation must certainly be looked upon as constituting the most characteristic one possessed by sugar. It was formerly thought, indeed, that a body which was susceptible of conversion into alcohol and carbonic acid in contact with yeast might be regarded as sugar, but the researches of modern times have shown that such a doctrine can be no longer held to be strictly true. It seems from the investigations of Berthelot, a French chemist of eminence who has devoted much attention to the chemistry of the sugars, and whose statements are entitled to the greatest consideration, that there are other substances, viz. glycerine, mannite, dulcine, and sorbine, which are capable of undergoing the alcoholic fermentation in contact with yeast. From this it would follow that the occurrence of the alcoholic fermentation cannot now be looked upon as affording an infallible indication of the existence of sugar.

For the application of the process of fermentation as a test for sugar, some sort of apparatus is needed. A contrivance that will be found to answer conveniently for the purpose is shown in the accompanying representation, fig. 4. To an ordinary test tube a tightly fitting cork is adapted, through which a piece of bent glass tubing passes, as shown in the sketch. The urine or other liquid to be examined is mixed with a moderate quantity of yeast and poured into the test tube until it is completely filled. The cork is then applied and forced into its place, taking care that no air is allowed to remain within the test tube. As represented in the drawing, one limb of the piece of bent tubing passes through the test tube until it very nearly touches the bottom. The apparatus, thus arranged, is now to be immersed in a vessel of tepid water. Should sugar be present evidence of fermentation will be very soon apparent. Carbonic acid gas is produced, and, rising to the top, drives out the liquid through the bent glass tube into a vessel placed for its reception.

FIG. 4.



Fermentation apparatus for the detection of sugar.

For ordinary purposes the evolution of gas may be taken as affording sufficient evidence of fermentation having occurred. If, however, it should be considered that actual proof is wanted, both the carbonic acid and alcohol produced may, without much difficulty, be chemically recognised by adopting the course to be described.

The test tube in which the experiment has been carried on, and in which the gas supposed to consist of carbonic acid has been collected, is to be inverted and the cork removed whilst its mouth is immersed under water. A small fragment of caustic potash is then to be introduced, and the thumb applied so as to close it.

It is next to be removed from the water and shaken freely. Carbonic acid being a gas which is absorbed by potash, it follows that if this should constitute the gas that has been generated, a vacuum will be formed in the interior of the test tube; and thus, on immersing the mouth of the tube a second time under water and removing the thumb, the water will rush up and occupy the space in the interior.

To detect the alcohol, the liquid in which the supposed fermentation has taken place is kept in a warm situation for the completion of the process to occur. It is then placed in a suitable apparatus and submitted to distillation. When about a third has passed over, this is taken and mixed with unslaked lime and placed in a test tube fitted with a perforated cork, through which a piece of glass tubing drawn out at one end to a pointed extremity passes. On the application of heat any alcohol that may be present is driven off in a tolerably pure form, and may be set light to as it escapes from the pointed extremity of the fine glass tube, when it will be found to burn with a pale blue flame, which is almost invisible in bright daylight. The water is detained by the lime within the test tube.

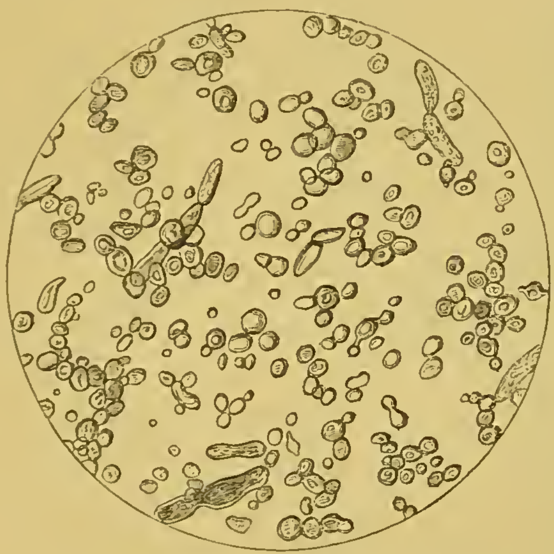
Another process, and a far more delicate one, for the detection of alcohol is with the bichromate of potash and sulphuric acid. To a moderately strong solution of bichromate of potash a little concentrated sulphuric acid is to be added. Chromic acid is liberated, and a deep red-coloured liquid produced. The first few drops of the product of distillation from the liquid supposed to contain alcohol are allowed to fall into the prepared fluid, and should alcohol be present it will assume with the aid of moderate warmth a beautiful emerald green tint. The alcohol exerts a de-oxidising influence on the chromic acid which the test contains.

In resorting to the use of the fermentation test it must be always borne in mind that yeast, as purchased, will by itself give signs, and even pretty strong signs, of the occurrence of fermentation. Where delicacy is required, the yeast, before being employed, should be washed with water, and the washing repeated three or four times, in order to get rid as far as possible of adhering starch and sugar. Even after this I have noticed the evolution of a slight amount of carbonic acid under exposure to trial in the fermentation apparatus. Unless, therefore, a marked result is obtained from the application of the test of fermentation, a counter-experiment should be set going in which the same quantity of yeast has been taken and treated with water only. A comparison must then be made of the amount of carbonic acid evolved in the two cases. Altogether, however, the fermentation test, it must be said, is not of that delicacy and facility of application as to render it a desirable one for ordinary employment. Its chief value is as a corroborative agent in cases of special import.

GROWTH OF THE TORULA CEREVISIÆ.

Urine containing sugar spontaneously undergoes in the course of a shorter or longer period, according to the temperature, the process of fermentation that has just been referred to; and with this, indeed the process is dependent upon it, the vegetable growth or fungus, which has been spoken of as constituting the yeast plant, or *Torula cerevisiæ* (the microscopic appearance of which is shown at fig. 5) becomes developed. The discovery of this fungus upon microscopic examination sometimes leads to the disclosure of the existence of sugar in specimens of urine where its presence had not previously been suspected. This is the reason that it is referred to here, for it is scarcely as an applicable test for sugar that the development of the *Torula cerevisiæ* can be spoken of—in the first place, because of

FIG. 5.



Sporules of *Torula cerevisiæ* (Hassall).

the uncertain time that elapses before the fungus may be recognisable; and next, because the *Torula cerevisiæ*, in its early or sporule stage of growth, that in which it is most frequently seen, so closely resembles another fungus, the *Penicilium glaucum*, that the two, it is asserted by good microscopists, cannot be safely pronounced as distinguishable from each other. The *Penicilium glaucum* is a very common fungus, being that which imparts the mildewed appearance so frequently presented by decaying vegetable and animal substances. It is not unfrequently encountered in certain specimens of urine, and has no relation to sugar.

THE QUANTITATIVE DETERMINATION OF SUGAR.

The sp. gr., it must be said, forms the criterion that is commonly appealed to in medical practice for supplying information respecting the amount of sugar contained in different specimens of urine. It is one, however, that gives at the best but a very rough and unreliable representation of what is wanted. Every one who is in the habit of determining, by one or other of the processes to be forthwith alluded to, the actual amount of sugar, and also of taking the sp. gr., is furnished with frequently recurring examples showing the want of harmony that may exist between the two, and therefore proving how fallacious a criterion the sp. gr. in reality is. There are other principles in diabetic urine to influence the sp. gr. besides sugar, and it is often found that specimens presenting the same or about the same sp. gr. are charged with widely different quantities of sugar; and, moreover, specimens are sometimes met with in which the amount of sugar differs, and it may be even to a considerable extent, in an inverse ratio to the density.

Estimation of sugar by the cupro-potassic solution.—The amount of sugar may be determined in several ways, but the method I prefer, and always adopt as being the quickest, and as yielding, I believe, the most correct result, is with the cupro-potassic solution the composition of which is given at page 14. The sugar is not separated and weighed, as the chemist so frequently serves an inorganic substance, but is estimated by its reducing effect upon the test solution, which is of an ascertained strength. It is, in fact, by what is termed volumetric analysis, a mode of analysis that has deservedly come of late into very extensive use, that the determination is carried out.

The cupro-potassic solution, accurately prepared according to the directions given, is of such a strength that 100 minims are just decolorised by half a grain of grape sugar: or, to put it in other words, the oxide of copper contained in 100 minims of the solution is all just reduced to the state of suboxide by the half grain of grape sugar. The valuation here given was obtained by actual examination with a specimen of grape sugar specially procured for the purpose, and weighed after having been thoroughly dried in a steam oven.

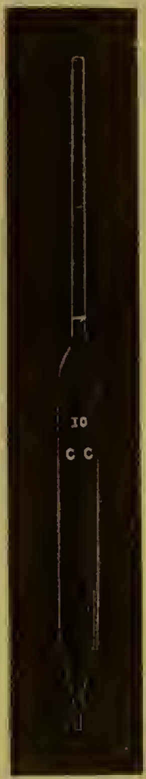
Fig. 6.

Graduated glass for dilution.

In order to represent the manner in which the analysis is performed, let us suppose that a specimen of diabetic urine is placed before us for examination, and recount the steps that are adopted.

In an ordinary uncontrolled case of diabetes the urine is too highly charged with sugar to operate with conveniently alone, and therefore it requires to be in the first place diluted to a known extent with water. For the process of dilution I generally use a tall narrow glass, such as is represented at fig. 6, which is graduated into 100 equal measures. The measures represent no particular quantity, all that is required being that they should be exactly equal to each other. Where there is reason to believe that the urine is in a highly saccharine state, it is best to dilute it with as much as four times its bulk of water. The glass, say, is to be filled up to 80 measures with water, and afterwards to 100 with urine. With urine in a less saturated state twice its bulk of water will suffice—60 measures, say, of water, and 30 of urine; or equal quantities may in some cases be taken, and sometimes even the urine will be best examined without dilution. The sp. gr. and amount of urine passed must serve, if no previous examination has been made, to give an idea of its degree of saturation and the extent of dilution that will be best. Before the analysis is made, the contents of the measure should be poured backwards and forwards into a glass once or twice, to secure that a thorough admixture has taken place.

FIG. 7.



Pipette for dilution.

FIG. 8.

100-minim graduated pipette.

Another convenient way of diluting is with the pipette shown at fig. 7. These pipettes are graduated to deliver a specific quantity, which is marked on them. One holding 10 c. c. may be used for the urine, and another holding either 20 or 40 c. c. for the water, according as the dilution is required to be carried to the extent of 1 in 3 or 1 in 5.

One hundred minims of the cupro-potassic test solution are now measured out into a small porcelain capsule, with the graduated pipette shown at fig. 8. Into the measured liquid a fragment of caustic potash about twice the size of a pea is dropped, for the purpose of causing the reduced oxide to fall in a denser form, so that the liquid may remain clear and allow the change of colour to be more readily seen. The capsule is then placed over the flame of a spirit lamp or gas, on a retort stand, or, what is better, on a piece of iron gauze adapted to the top of a stoneware cylinder, as is seen arranged at fig. 9. The cylinder protects the flame

FIG. 9.

Arrangement for estimating the amount of sugar by the cupro-potassic solution.

from draught, and the gauze distributes and regulates the heat, and causes the contents of the capsule to boil more steadily.

The 100-minim graduated pipette (fig. 8) is again brought into use for ascertaining the amount of the liquid being examined that is required to decolorise the cupro-potassic solution contained in the capsule. It is filled so as to start on a line with 0 on the scale; and, directly boiling has commenced in the capsule, its contents are allowed to fall drop by drop into the copper solution, which must be kept quietly boiling all the while, and moved about gently by tilting the capsule from side to side with a glass rod, until all appearance of blue has been removed. What is wanted is just to get a removal of all trace of blue, and no more; and as soon as this has been attained the escape of liquid from the pipette must be stopped, and the amount that has been used read off from the graduated scale.

Usually, when the operation is properly performed, the red oxide slowly collects as it is produced at the bottom of the capsule, leaving the liquid above perfectly clear, and thus, in such a state that the gradual disappearance and final loss of colour may be with precision observed. At other times, however, the reduced oxide, instead of settling as has just been said, is deposited in a more or less diffused form through the liquid, obscuring, to a certain extent, its behaviour, but still not preventing, after a little experience, the point that is looked for being seen. All trace of blue and green should be just destroyed, and a pure orange or orange-red produced. By tilting the capsule a little on one side from time to time a thin stratum of liquid is brought over the clean white surface, and in this way any appearance of remaining blue is more readily discerned.

The pipette that has been referred to is graduated in minims according to the Pharmacopœia standard—that is, each minim is equivalent to the $\frac{1}{480}$th part, by measure, of a fluid ounce. The scale begins from above so that when the start has been made from 0 the amount that has been used for producing the result required can be read off at a glance. The pipette here described is supplied by Messrs. Griffin and Sons, of 22, Garrick Street, Covent Garden, from whom, also, all the other apparatus that has been referred to can be obtained.

For the sake of illustration, let it be supposed that ten pints of urine have been passed by a diabetic subject in the twenty-four hours. To obtain an accurate knowledge of the amount of sugar voided during this period, the urine must be all mixed together, and the specimen for examination taken from the whole. The necessity of adopting this course arises from the fact that the urine passed at different periods of the twenty-four hours is charged, as will be subsequently seen, to a very variable extent with sugar. The urine is diluted to the extent, say, of 1 part in 5. One hundred minims of the cupro-potassic solution are next measured out into the capsule, and the fragment of caustic potash dropped in. The capsule being then placed over a flame and gentle boiling induced, the diluted urine is dropped from the pipette, previously charged up to a line with 0 on the scale, until the required decolorisation is effected. The escape of diluted urine from the pipette is controlled by the finger applied to the top of the tube, as shown at fig. 9; and, directly the required change has been produced, its further escape is stopped, and the amount that has been used read off from the scale. Say that twenty-eight minims are found to constitute the quantity that has been employed, we have now all the information that is wanted from the process, and a little calculation will suffice to reduce the result to intelligible figures.

As 100 minims of the cupro-potassic solution take half a grain of sugar for their decolorisation, and as 28 minims of the diluted urine produced that result, it follows that the 28 minims of diluted urine are equivalent to, or contain half a grain of sugar. A simple rule of proportion sum will give the amount of sugar contained in the fluid ounce; thus—

	Minims of diluted urine.		Grains of sugar.		Minims of diluted urine.		Grains of sugar.
As	28	:	·5	: :	480 (one fluid ounce)	:	8·57

8·57 grains, then, form the quantity of sugar contained in a fluid ounce of the liquid examined. Now, this consisted, not of pure, but of diluted urine, the extent of dilution being one part of urine with four of water. The composition of the liquid being thus one part of urine in five, the 8·57 grains must be multiplied by 5 to get the amount of sugar ($8{\cdot}57 \times 5 = 42{\cdot}85$) contained in a fluid ounce of undiluted urine. This requires now to be multiplied by the number of ounces of urine voided, and the quantity of sugar eliminated during the twenty-four hours is given. Ten pints, or 200 ounces, was the quantity of urine put down as having been passed; therefore 42·85 have to be multiplied by 200, and we get 8570 grains, or something over the avoirdupois pound, which consists of 7000 grains, as the amount of sugar discharged.

After a little practice this process may be performed in a much shorter time than it takes to describe it. With all that is wanted conveniently at hand, a few minutes amply suffice for its completion. It is a process which, like testing for albumen and taking the sp. gr., may be readily performed during the interview with a patient in the consulting room; and it is fortunate that such is the case, for without a knowledge of the amount of sugar that is being passed I consider but an imperfect notion can be had regarding the precise form and progress of the disease.

It is not always convenient to a patient to bring a mean specimen of the urine that has been passed during the twenty-four hours. If this can be done it is desirable, as the information derived from its examination is much more exact and complete than can otherwise be had. Where a mean specimen for the twenty-four hours is not brought it is best to desire a patient to bring a portion of what is passed on going to bed at night—not *during* the night, but simply that which is passed the last thing before going to bed. I ask for this particular specimen because it forms about the worst in respect of saturation with sugar. The urine at this period is under the influence of the food that has been consumed during the day, and the difference between it and that which is passed the first thing in the morning is oftentimes exceedingly marked. To examine specimens brought without any fixed rule as to period of collection gives but an unsatisfactory result, on account of the sugar varying in quantity, as it will be subsequently shown to do in the urine voided at different periods of the twenty-four hours.

That the process I have just described is susceptible of yielding a result presenting not only a fair but even a minute degree of accuracy I have proved upon several occasions. In the case of North, reported in full at the end of this work, whilst the effect of different articles of food was being ascertained the urine was collected separately for every four hours during the day and night, and the quantity of sugar passed during each period determined. The several portions of urine (excepting, of course, the small quantity that had been withdrawn from each for analysis) belonging to the twenty-four hours, were then mixed together, and a specimen drawn from the whole was examined, in order to check the results obtained from the separate analyses. The amounts yielded by the two processes presented a very close respondence with each other.

To avoid having to go through the calculation upon each occasion, for ascertaining the amount of sugar present per ounce from the number of minims taken to decolorise the measured quantity of blue liquid, I have worked out the results and placed them together in the form of table, which will give at a glance the information required. Suppose, for instance, 26 minims to have formed the quantity of the liquid examined that was required to decolorise the 100 minims of test solution; all that is necessary is to look opposite 26 in the accompanying table, and the amount of sugar present per fluid ounce will be found. It happens to be 9·23. These figures, of course, represent the quantity per ounce contained in the liquid that has been actually submitted to examination; and if this has consisted of diluted urine, they must be multiplied according to the extent of dilution that has been performed to get the quantity of sugar contained in the urine itself. Should the liquid examined have consisted, say, of 1 part of urine with 4 of water, the 9·23 will have to be multiplied by 5, and 46·15 grains ($9{\cdot}23 \times 5 = 46{\cdot}15$) will be given as the amount of sugar present in each fluid ounce of undiluted urine.

Table representing the quantity of sugar per fluid ounce corresponding with numbers of minims, ranging from 15 *to* 100, *required to decolorise* 100 *minims of the cupro-potassic test solution.*

Minims to decolorise.	Sugar per fluid ounce.	Minims to decolorise.	Sugar per fluid ounce.	Minims to decolorise.	Sugar per fluid ounce.
15	16·	44	5·45	73	3·28
16	15·	45	5·33	74	3·24
17	14·11	46	5·21	75	3·20
18	13·33	47	5·10	76	3·15
19	12·63	48	5·	77	3·11
20	12·	49	4·89	78	3·07
21	11·42	50	4·80	79	3·03
22	10·90	51	4·70	80	3·
23	10·43	52	4·61	81	2·96
24	10·	53	4·52	82	2·92
25	9·60	54	4·44	83	2·89
26	9·23	55	4·36	84	2·85
27	8·88	56	4·28	85	2·82
28	8·57	57	4·21	86	2·79
29	8·27	58	4·13	87	2·75
30	8·	59	4·06	88	2·72
31	7·74	60	4·	89	2·69
32	7·50	61	3·93	90	2·66
33	7·27	62	3·87	91	2·63
34	7·05	63	3·80	92	2·60
35	6·85	64	3·75	93	2·58
36	6·66	65	3·69	94	2·55
37	6·48	66	3·63	95	2·52
38	6·31	67	3·58	96	2·50
39	6·15	68	3·52	97	2·47
40	6·	69	3·47	98	2·44
41	5·85	70	3·42	99	2·42
42	5·71	71	3·38	100	2·40
43	5·58	72	3·33		

By multiplying the figures representing the amount of sugar per ounce by the coefficient ·23, the quantity of sugar may be reduced to a per-centage proportion. Thus, suppose a specimen of urine to contain 36 grains of sugar to the ounce, then 8·28 grains (36 × ·23 = 8·28) will be given as forming the amount per cent.

Estimation of sugar by the alkali test.—Vogel (Neubauer and Vogel 'On the Urine,' Sydenham Soc. Translation) says, in reference to this as a quantitative test—" In consequence of the difficulty attending the employment of the methods mentioned for determining the quantity of sugar in urine, I have proposed another process, which, however, gives only approximative, but not absolutely accurate, results. It is simple, and, as a rule, fully sufficient for all the purposes of the physician, who in most cases requires only to ascertain, there or thereabouts, the quantity of sugar in the urine, and whether the quantity increases or diminishes. The process is founded on the fact that saccharine urine, when boiled with caustic potash, assumes a yellowish-brown colour, and that from the intensity of the colour the quantity of sugar may be determined by means of a scale of colours in the same way as the pigment matter of the urine."

Dr. Garrod recommends a solution of carbonate instead of caustic potash as the agent for employment. A colour standard is first to be prepared by boiling a known quantity of sugar with the carbonate of potash solution. This is then placed in a clear glass tube of about half an inch in diameter. A measured quantity of the urine to be examined is next boiled with the test for five minutes, introduced into a graduated tube of the same diameter as the other, and diluted with water until its tint corresponds with that of the standard. By ascertaining the amount of dilution required for the production of this result, the quantity of sugar in the urine examined can be found.

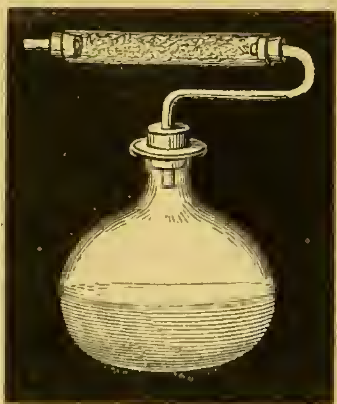
The same must be said, in my own opinion, about this as a quantitative, as what has been said about it as a qualitative, test—namely, that it is not to be compared in value to the cupro-potassic solution.

Estimation of sugar by fermentation.—Fermentation may be applied to the quantitative determination of sugar in two ways. Either the amount of carbonic acid evolved, which will be in proportion to the amount of sugar present, may be ascertained by weight or volume; or, as suggested by Dr. Roberts, the loss of density occurring as the result of the disappearance of the sugar may be turned to account for estimating its amount.

The weight of the carbonic acid evolved may be ascertained by causing it to pass through a solution of potash in a Liebig's potash tube, after being dried by passage through a chloride of calcium tube or a tube containing fragments of pumice stone moistened with strong sulphuric acid, and noticing how much increase in weight the potash tube acquires.

Another, and perhaps a more simple, plan for determining the weight of the carbonic acid evolved, is by allowing it to escape and ascertaining the amount of loss that occurs. Fermentation is carried on in the form of apparatus depicted in the accompanying figure (fig. 10). The carbonic acid produced in the flask is made to pass through a tube containing chloride of calcium or fragments of pumice stone moistened with sulphuric acid before it

Fig. 10.



Apparatus for estimating the loss by weight of carbonic acid from fermentation.

escapes. By this means the watery vapour is detained, and nothing but carbonic acid allowed to pass out. The apparatus and its contents being weighed before and after fermentation, a difference is observed which indicates the amount of carbonic acid that has been evolved. For each grain of carbonic acid about two grains of grape sugar are to be reckoned.

To estimate the amount of carbonic acid by volume, fermentation must be performed in a graduated tube over mercury. Each cubic inch of gas evolved may be taken as representing, in round numbers, one grain of sugar, forty-seven cubic inches of gas being the precise volume, according to Dr. Christison, produced by forty-five grains of grape sugar.

The difference observable in the density of a saccharine liquid before and after the destruction of its sugar by fermentation, has been ingeniously turned to account by Dr. Roberts, of Manchester, for a quantitative analytical purpose. As a saccharine liquid loses its sugar by fermentation, its density is found to fall. The fall in density that takes place arises from two distinct but nevertheless associated causes—first, the disappearance of the sugar; and next, the presence of generated alcohol. Now, the loss of density from these causes, as Dr. Roberts states, must stand proportional to the quantity of sugar originally present, and must consequently furnish a measure of such quantity. Every degree of "density lost" he has found by experimental observations to form the representative of one grain of sugar to the fluid ounce. For the practical application of the method to the examination of diabetic urine, the following are the directions he has given:—

"About four ounces of the saccharine urine are put into a twelve-ounce bottle, and a lump of German yeast about the size of a cobnut or small walnut is added to it. A great excess of yeast is added to hasten fermentation, but a little more or a little less does not sensibly affect the result. The bottle is then covered with a nicked cork (which permits the escape of the carbonic acid), and set aside on the mantelpiece or other warm place to ferment. Beside it is placed a tightly corked four-ounce phial filled with the same urine without any yeast. In about twenty-four hours the fermentation will have ceased, and the scum cleared off or subsided. The fermented urine is then decanted into a urine-glass, and its specific gravity taken; at the same time the density of the unfermented urine in the companion phial is observed, and the density lost [*i. e.* the difference of density between the two] ascertained. Fermentation is generally complete in about eighteen hours if the locality be sufficiently warm; and it is desirable to remove the two phials into a cool place two or three hours before the densities are taken, in order that they may attain the temperature of the surrounding atmosphere."

Suppose that the above-described process has been put into force and that the density of the fermented specimen is found to be 1006, whilst that of the unfermented one stands at 1040; then thirty-four grains will have to be put down as forming the quantity of sugar per fluid ounce. Should the urinometer be used for taking the sp. gr., attention must of course be paid to secure that an instrument is employed which registers correctly.

This process of Dr. Roberts, looking upon it as yielding a correct and constant result, certainly possesses the advantage of being so easy of application that the patient or his friends may be entrusted to perform it, but it has also the disadvantage of requiring a considerable length of time to elapse before the result can be ascertained.

Estimation of sugar by polarisation.—When a ray of polarised light is made to pass through certain solutions it is found to emerge still in a polarised state, but polarised in a plane different from that which belonged to it before entering. With some solutions the plane of polarisation is turned to the right, with others to the left. This constitutes the phenomenon to which the name of circular polarisation has been given.

Diabetic sugar possesses the property of turning the plane of polarisation to the right, and the extent of rotation produced is in proportion to the amount of sugar that is traversed. Now, this, it follows, will depend upon two conditions — the length of the column of liquid employed, and the degree of concentration of the solution. By maintaining either of these conditions constant, any variation observed must be dependent upon a difference in the other. Hence, if a ray of polarised light be transmitted through tubes of equal length filled with different specimens, say, of saccharine urine, and a variation in the extent of rotation is noted, it must be upon a difference in degree of saturation that such variation is dependent. Now, not only will the rotation be influenced by the degree of saturation with sugar, but the two will be in a direct ratio to each other. A certain number of degrees of rotation, for instance, will be produced by a specimen containing a given amount of sugar, and double the number of degrees of rotation by another specimen that is charged with double the amount of sugar. By operating upon specimens of known strength the value of the degrees of rotation can be ascertained, and in this way does circular polarisation become available for estimating the amount of sugar in liquids containing an unknown quantity.

Instruments are constructed by which the rotation of the plane of polarisation is rendered susceptible of easy observation, and a scale is affixed whereby the extent can be measured. The polarising saccharimeter is the name given to the instrument in question. It is procurable at Messrs. Elliott, Brothers, in the Strand, and other philosophical instrument makers, at the cost of a few pounds. Although considerably used in France for ascertaining, for certain purposes, the strength of saccharine liquids, in England the instrument is not much known. The colour of the urine offers the chief obstacle to its application in diabetes. To the medical practitioner expert in chemical testing its want is not felt, but to the patient it might be sometimes found an acquisition as affording a neat means of enabling him to watch his own case through the medium of the quantity of sugar that is being passed.

ON THE

PHYSIOLOGICAL RELATIONS OF SUGAR.

Sugar, the escape of which from the system with the urine forms the great characteristic feature of diabetes mellitus, constitutes a material which enters into the composition of our food, and has a part to play in the economy of life. This being the case, a study of the physiological relations of sugar is called for preparatory to discussing the pathology of diabetes.

Sugar as an alimentary principle is derived from the vegetable kingdom, in which it forms a pretty abundant product. Its properties are such that it requires to undergo no digestion or preparatory process for absorption. Being of an exceedingly soluble and diffusible nature, it can readily pass, simply in compliance with physical laws, from the alimentary canal into the blood-vessels. The villi form the special absorbing organs of the alimentary tract, and have an absorbing power over certain portions of our food which cannot be explained by physics. They pick up oleo-albuminous matters and discharge them into the lacteal system, by which they are transmitted to the thoracic duct, and thence poured into the general venous circulation of the body. With a diffusible principle like sugar no special absorbing action is required for its passage into the system. In compliance simply with the laws of osmosis, it reaches the interior of the blood-vessels ramifying upon the surface of the alimentary canal. From these it is conducted, not at once into the general circulation, as is the case with the matters absorbed by the lacteals, but through the portal system of veins to the liver. This, as will be subsequently seen, is a point of importance, for it can be shown that the liver arrests it and transforms it (this transformation constituting its first step of assimilation) into a body which has received the name of amyloid substance.

There is another substance in our food which is analogous to sugar, and which exists still more largely than sugar as a vegetable product. The substance I allude to is starch, a substance which, although presenting very different chemical and physical properties from sugar, is transformable into it, when the requisite conditions are supplied, with the greatest facility. Starch, it may be considered, as long as it remains as such, is of no use either to the animal or vegetable organism. It forms a convenient storage material, which may be kept for an indefinite period without undergoing alteration. To be applicable to the purposes of life it must first be converted into sugar, and this is effected by the influences to which it is subjected on being placed in a position for requirement. Grains of wheat, for instance, which have been excavated with mummies of ages past, are found to retain their starch in an unchanged state. By exposure to warmth, air, and moisture, the three essential conditions of active life, these grains of wheat start into growth, and their starch undergoes transformation into sugar. The circumstances which call it into requisition lead to its transformation in such a manner as to render it susceptible of being applied to the purposes of life. In the animal also provision is made for its transformation into sugar as a preliminary step to its employment. Without this transformation it will pass through the alimentary canal unabsorbed, and thus prove useless to the economy.

Diastase, a principle developed during germination, constitutes the agent that excites the transformation of starch in germinating grain. By its influence the starch is metamorphosed, first into dextrine, and then into sugar.

It will subsequently be shown, in respect of the animal organism, that because a quantity of sugar is to be found in the liver after death it must not be concluded that the same is the case during life; and so it may be said with regard to malted grain—that is, grain which has been allowed to germinate and then exposed to heat—the quantity of sugar found in it must not be taken as an index of that contained in it during the actually growing and living state. On allowing, for instance, barley to germinate fully to the extent that is done in malting, and then making a cold infusion of it, I have found that but a very slight indication of the presence of sugar is yielded. In the process of malting the germinating grain is subjected to a kind of partial roasting on the kiln, and it is here, instead of in the natural act of germination, that the large amount of sugar encountered in malt is produced. The diastase developed during germination, like other fermentative principles, acts with greatly increased energy at an elevated temperature, and this it is to which the large amount of sugar met with in malt is to be attributed.

Should barley, however, it may be mentioned, be allowed to grow much beyond what is permitted in malting, then a marked indication of the presence of sugar may be encountered without the artificial exposure of the grain to the influence of an elevated temperature.

In the animal organism starch is converted into sugar by secretions poured for this, as one of their purposes, into the alimentary canal. Human saliva has the power of rapidly transforming starch into sugar. With a decoction of starch and at the temperature of the living body a few moments' contact suffice for sugar in quantity to appear. It happens, however, that the saliva does not in the case of all animals enjoy a similar property. In the horse and dog, for instance, the pure secretions of the different salivary glands, singly and mixed together, fail to possess the power when fresh of transforming starch into sugar. It is true, after they have been kept for a few days they do so; but in this there is nothing special, the property being one that is common to organic fluids in general in a state of decomposition. What has been stated applies only to the secretions obtained direct from the salivary glands, for the mixed saliva collected from the mouth of these animals is found to possess some amount of transformative power, although nothing like the same amount that is enjoyed by the saliva of the human subject.

Looking at these and other considerations, it may be inferred that, although our own saliva possesses the metamorphosing power that has been mentioned, yet this is not the secretion that is designed by nature for effecting the conversion of starch into sugar. It is seldom that starch is received into the mouth in the form of food under as favorable a state for transformation as it is in the decoction that may happen to be experimented with outside the body. The mouth is not a part of the digestive tract in which the food is long delayed, and any action that may be here commenced will be checked as soon as the stomach is reached and its acid secretion come in contact with, for experiment shows that the presence of an acid, and a very small quantity suffices for the purpose, renders saliva inoperative as a transformative agent over starch.

The small intestine it may be said forms the part of the digestive tract in which the conversion of starch into sugar is mainly, if not almost entirely, effected. The pancreatic juice, the intestinal juice, and it may be considered also the secretion of Brunner's, or the duodenal glands, all possess in a high degree a transformative power. In the intestine, unlike as in the mouth, everything is favorable to the occurrence of metamorphosis. The food, for instance, has been reduced to a semifluid state before being brought in contact with the secretions. The acidity of the contents of the stomach soon becomes more or less completely neutralized after the intestine is reached. By means of the intestinal peristalsis the alimentary matters and the secretions are thoroughly incorporated together as they are urged slowly along the canal. Thus circumstanced, and exposed also to the elevated and equable temperature existing in the centre of the body, the starch is placed under the most favorable conditions for transformation into sugar, and as the transformation is effected the sugar is absorbed by the blood-vessels and carried to the liver.

We have, then, to deal with sugar that has been introduced as such with the food and with sugar that has been derived from the metamorphosis of starch within the alimentary canal. The result in both cases is the same. The sugar passes from the alimentary canal into the vessels of the portal system, and is thence conveyed to the liver.

Such was the extent of knowledge that had been obtained when the experiments of Bernard were commenced, which have opened out a new field of inquiry upon the subject. Desirous of ascertaining how far the sugar absorbed from the alimentary canal could be traced within the circulatory system, Bernard experimented upon animals to which he had purposely administered food containing a plentiful supply of saccharine matter. He examined the contents of the circulation at different points, and arrived at the conclusion that the sugar passed through the liver and then pursued its course along the inferior cava and through the right heart to the lungs. Here he thought the sugar was destroyed, for in his experiments only a traceable amount was discoverable in the blood of the arterial system—that is, blood which had just been derived from the lungs—whilst the blood removed from the right cavities of the heart, or that on its way to the lungs, gave evidence of containing a large amount.

Now, to verify the conclusions he had arrived at Bernard thought it advisable to perform a counterpart experiment and see that an absence of sugar, where it had been previously met with, existed when its introduction with the food was withheld. Accordingly he operated on a dog that had been for some time restricted to a diet of animal food, and to his astonishment still found sugar in the blood derived from the right side of the heart. Thus was laid the foundation for an inquiry out of which has sprung such unlooked-for results.

The question immediately arose, what was the source of the sugar that had here been encountered? The current of blood was followed backwards, and it was ultimately found that it came from the liver, and hence originated the conclusion that the liver discharged a sugar-forming function in addition to its office of secreting bile.

It was in 1848 that Bernard published his discovery, which took physiologists by surprise and soon became known far and wide. Nothing could seem to be wanted of a more conclusive nature than the well-known experiment upon which he based his glycogenic theory. An animal, after having been for some time previously restricted to a diet devoid of starch and sugar, was killed, and specimens of blood collected from the portal and the hepatic veins for chemical examination. That from the portal vein (blood flowing towards the liver) was found upon analysis to be free from sugar, whilst that from the hepatic vein (blood flowing from the liver) contained it in quantity. The liver, also, to the exclusion of all other organs of the body, presented a marked saccharine behaviour. From the quantitative examinations that were made it was stated that sugar existed in the blood of the hepatic vein to the extent of about 1 per cent. during fasting, and from $1\frac{1}{2}$ to 2 per cent. at a period of full digestion. The mean quantity found in the liver was said to be $1\frac{1}{2}$ to 2 per cent. The process of sugar formation thus appeared to be carried on upon an extensive scale, and hence might reasonably be looked upon as contributing to some important purpose in the economy of animal life.

Now, this experiment certainly shows beyond all question, contrary to the notion that was previously entertained, that sugar can be produced in the animal organism without any vegetable principle being concerned. It was formerly thought that sugar formed an article that was producible only by the vegetable kingdom, but it now became evident that such a doctrine could no longer be upheld. The question, however, that will have to be entered upon presently—and it is a question of considerable interest to the physiologist, and also to the pathologist with regard to diabetes—is not whether sugar *can* be formed by the animal kingdom, but whether its production occurs as a natural phenomenon of life in accordance with what was inferred from the experiment of Bernard.

The next step in the history of animal glycogenesis was the discovery and isolation of the principle from which the sugar takes origin in the liver. It was first of all ascertained that the production of sugar might be shown to occur after death had taken place. Bernard passed a stream of water through the vessels of the liver of a recently killed animal until all the sugar with which it was impregnated was washed out—this being proved by the subjection of a specimen to the appropriate chemical examination. He then placed the organ aside and examined it again after the lapse of some hours, and found that it had re-acquired a strongly saccharine character. It thus became evident that the production of sugar must be attributable to some simple chemical change, and not to any special action of life.

The actual source of the sugar remained still to be disclosed; but whatever the principle from which it was formed, it was clear that it must consist of something less soluble and less diffusible than sugar, or otherwise it would have been washed away with this material by the stream of water that was passed through the liver. It was in 1857 that the announcement was made that the isolation of the sugar-forming material had been effected; and as sugar-formation was supposed by Bernard to constitute its physiological purpose, it was named by him glycogenic matter or glycogen. The glycogenic theory was considered to remain unaltered by the discovery of this substance, except in so far as to be placed upon a more satisfactory footing by the disclosure of a recognisable source for the sugar.

Respecting the name given to this newly discovered material, something requires at once to be said. I must protest, for reasons that will afterwards appear, against the employment of the term that was made use of by Bernard, if it is to be regarded as implying, as it was proposed for doing, its physiological destination. It is true that, after death and under certain unnatural conditions, it is a *glycogenic* or sugar-forming substance, but sufficient evidence will, I think, be advanced to show that, under natural circumstances, such is not the case. "Amyloid substance" is a name that has more recently been given to it, and by this it is now very generally called. The term simply implies, as is the truth, that it is a body presenting an alliance to starch. There is this misfortune, however, with regard to this appellation, viz. that the term "amyloid matter" has been applied by Virchow to a totally different material —a product of disease which seems to contain nitrogen, and, therefore, to have no real title to be so called. In using the term "amyloid substance," it is consequently necessary not to confound the material under consideration with the so-called "amyloid matter" of disease. At one time I suggested the name of "hepatine;" but as it has since been found that the substance is not by any means exclusively encountered in the liver, it is not advisable that it should be retained. Zoamyline is still another name that has been given to it, and is by some authorities employed.

Amyloid substance, as I shall elect to call the material under consideration, has for its seat in the liver the hepatic cells—at least, such may be inferred from what is observed under micro-chemical examination. As it is rarely met with in the liver when death has taken place from disease, but is always present under healthy circumstances, its production may be looked upon as constituting one of the natural operations of the cell.

For extracting the amyloid substance from the liver, a very simple process suffices. Let a piece of the organ, taken from a recently killed healthy animal, be plunged for a few minutes into boiling water so as to destroy the ferment that is present and prevent any further loss of the substance by transformation into sugar. It is then to be well pounded in a mortar, treated with a moderate quantity of water and thoroughly boiled. The decoction thus procured, after having been strained or filtered, is poured into about five or six times its bulk of spirit, by means of which the amyloid substance is thrown down as a dense white precipitate. This may now be collected on a filter, washed with spirit, and dried.

Amyloid substance, as thus obtained, is free from contamination with sugar, but not actually pure. It is, however, quite sufficiently so for studying the characters it possesses. To obtain it in a state of chemical purity it may be dissolved and boiled in a strongish solution of caustic potash. The potash destroys the impurities without acting upon the amyloid substance. The solution being poured into spirit, the amyloid substance is again thrown down, and requires to be re-collected on a filter and well washed with spirit. The organic impurities are thus removed, but it is found to cling so tenaciously to the potash that has been used that no amount of washing seems to be capable of effecting a complete separation. By re-dissolving, however, in water and adding acetic acid beyond the neutralizing point, the amyloid substance, when again thrown down by alcohol, is thoroughly freed from the potash; and, after a little washing on a filter to remove the acetate that has been formed and the excess of acid employed, it may be regarded as in a state of chemical purity.

The property enjoyed by amyloid substance of resisting the action of a boiling solution of potash, and of being precipitable by spirit, may be advantageously turned to account for separating it from other matters and effecting a quantitative determination in any given specimen of liver. It was in this way that the quantitative determinations to be furnished further on were made. A piece of liver, for example (about 200 grains forms a convenient amount for operating upon), was taken, and, after its weight had been noted, was pounded in a mortar with some caustic potash in a solid state. About two thirds the weight of the liver employed formed the quantity of potash used. A little water having been added, the whole was carefully transferred to a small porcelain capsule and boiled for several minutes, or until complete solution was observed. The liquid was then poured into about six times its volume of spirit, by which the amyloid substance was thrown down as a white flocculent precipitate. The precipitate was allowed to subside and the liquid drawn off with a pipette and fresh spirit added, and this process repeated a few times. Finally, the precipitate was collected on a filter, still further washed, and afterwards dried and weighed. It is true, as has been mentioned, the precipitate thus obtained does not consist of amyloid substance in an absolute state of purity, but the result yielded by the process may without hesitation be accepted as quite near enough the truth for all physiological purposes.

In its chemical properties amyloid substance presents alliances to both starch and dextrine, but resembles the latter, it may be said, more strongly than the former. It constitutes a neutral, colourless, tasteless, inodorous, and uncrystallizable body. It is largely soluble, although not rapidly so, in water, the solution presenting an opaquely lactescent character. As regards this lactescence, it is a curious fact that a certain amount of dilution is required for its production—in other words, in a highly concentrated state the solution is clear, but becomes lactescent when water is added. When its solution is boiled a scum collects upon the surface, and if this scum (which consists of amyloid substance) be removed and allowed to dry spontaneously, it forms a semi-transparent, hard, brittle, and gum-like or resinoid body. It is insoluble in alcohol and glacial acetic acid, and by both these agents may be precipitated from its aqueous solution, the precipitate assuming, when dry, a white pulverulent form. It is unaffected, as already mentioned, even at a boiling temperature, by the caustic alkalies, but boiling for a short time in contact with a mineral acid leads to its transformation into sugar. Its susceptibility of undergoing transformation into sugar must be regarded as forming one of its most noteworthy properties; and, besides boiling with a mineral acid, contact with many animal products, which we look upon as ferments, will also bring it about. For instance, saliva, pancreatic juice, blood, liver-tissue, &c., are found to constitute energetic agents in effecting its conversion into sugar. Its behaviour with iodine resembles that of dextrine, the reaction obtained being the production of a deep wine-red coloration. As long as it exists as amyloid substance it gives no reaction with the copper, fermentation, or any other sugar test.

Amyloid substance is admitted to be devoid of nitrogen, and to constitute a body belonging to the carbohydrate group. Bernard gives as its formula $C_{12}H_{12}O_{12}$, which is derived from the analysis of E. Pelouze, the result of which is represented to have been as follows:

Composition of amyloid substance (E. Pelouze):

Carbon . . .	39·8
Hydrogen . . .	6·1
Oxygen . . .	54·1
	100·0

It should be stated that some analyses which have been made by others do not strictly accord with what is to be found above. My former colleague, Dr. Odling, undertook the ultimate analysis of four specimens of amyloid substance procured from a rabbit's liver, and specially prepared by myself, in different ways, for the purpose. The results he obtained, as will be seen, more closely correspond with the result of an analysis made by Prof. Apjohn, of Dublin, than with the figures given by Pelouze.

Specimen No. 1. Prepared by precipitation and washing with alcohol only. The composition yielded was as follows:

Carbon . . .	42·68
Hydrogen . . .	6·47
Oxygen . . .	50·32
Nitrogen . . .	·53
	100·00

Specimen No. 2. Precipitated and washed with spirit, after having been boiled with dilute hydrochloric acid. Result obtained:

Carbon . . .	43·24
Hydrogen . . .	6·38
Oxygen . . .	49·99
Nitrogen . . .	·39
	100·00

Specimen No. 3. Prepared in the same way as No. 2, excepting that it was boiled with glacial acetic acid instead of hydrochloric acid. Composition given:

Carbon . . .	42·80
Hydrogen . . .	6·15
Oxygen . . .	50·58
Nitrogen . . .	·47
	100·00

Specimen No. 4. Treated by boiling with a strong solution of potash for half an hour, and then precipitated and washed with alcohol. Result yielded:

Carbon . . .	42·97
Hydrogen . . .	6·63
Oxygen . . .	50·29
Nitrogen . .	·11
	100·00

The nitrogen in all these specimens may be regarded as an accidental impurity, and it will be observed that it was smallest in the specimen that was boiled with potash, or treated in the manner most effectual for removing it.

The following is the result that has been referred to as having been obtained by Professor Apjohn. The specimen examined was procured from the livers of rabbits, and prepared for analysis by Dr. McDonnell:

Carbon . . .	43·78
Hydrogen . . .	6·32
Oxygen . . .	49·28
Nitrogen . . .	·62
	100·00

"Neglecting," Professor Apjohn says, as quoted by Dr. McDonnell ('Observations on the Functions of the Liver,' Dublin, 1865), "the trace of nitrogen as an accidental impurity, I find that these results are very accurately represented by the formula $C_{12}H_{10}O_{10}$, which is that representing the constitution of starch and dextrine."

Having brought the consideration of the subject up to this point, the fitting moment has arrived for discussing the question of validity of the glycogenic theory—for inquiring, in other words, whether sugar is produced by the liver, and poured into the circulatory system, as a natural phenomenon of life, in accordance with the inference that has been drawn from the experimental results that have as yet been referred to.

M. Figuier contended that no sugar was to be found in animals unless introduced from without by means of a saccharine or amylaceous alimentation. The flesh of the vegetable feeder consumed by the carnivorous animal, he maintained, contained sugar, and the sugar encountered in the liver he believed to be derived from this source. Thus, in the carnivorous as well as the herbivorous animal, he was of opinion that sugar was conveyed to the liver by the portal blood, and was simply picked out and stored up by the organ, instead of being formed by it. The reason assigned for no sugar being recognisable in the portal blood, was that its presence was masked by the existence of some unknown principle. In answer to these assertions of M. Figuier it was not difficult for Bernard to show that they were based upon an untenable foundation.

M. Sanson was the next to stand forward as an opponent to Bernard's glycogenic theory. Like M. Figuier, he considered that there was only one source for the sugar met with in the animal system: that this was from without, and ultimately the vegetable world. The amyloid substance or glycogen of Bernard he looked upon as nothing but dextrine, which formed a constituent, he asserted, of blood and flesh as well as the liver. The liver was not an organ for producing the glycogen, but merely for abstracting it from the blood, and transforming it into sugar with greater activity than was elsewhere done. "The herbivora," said Sanson, "find the amylaceous principle in their food. This they transform into dextrine; one portion of which they use, the other accumulates in the tissues. The carnivora find in this accumulated dextrine the source of their sugar without having to elaborate it."

The report made to the Académie de Médecine by a commission composed of MM. Bouley, Poggiale, and Longet, appointed to inquire into this view, stands opposed to the assertions of M. Sanson. In dogs fed upon flesh no amyloid substance was found, except in the liver. Amyloid substance was met with also only in the liver of the herbivora, except when these animals were fed upon a diet rich in amylaceous materials. As the result of a large number of examinations, amyloid substance was only once encountered in butcher's meat, but constantly found in the flesh of horses. In harmony with this last remark it may be mentioned that Sanson's original experiments were conducted upon horses at the Veterinary School of Toulouse.

In the observations conducted in my own laboratory upon dogs restricted to an animal diet, the lung and muscular tissues have yielded a small quantity of a substance which was coloured red with iodine, and convertible into sugar by the action of saliva—a substance, therefore, presenting the characters of amyloid substance and dextrine. None, however, was furnished by the spleen, pancreas, or kidney, and as regards the blood, certainly in the case of the dog, my own experience is in direct antagonism with the assertion of M. Sanson.

I am now brought to the grounds upon which I have myself been led to call in question the validity of the doctrine of glycogenesis, and it will be seen that they are of a totally different nature from those which have been as yet referred to. I may state at the outset that I have nothing to say against the accuracy of the facts—taking them simply as facts—that have been put forward by Bernard. Repeating Bernard's experiments, as he performed them, results are to be obtained, as I can personally testify, in strict accordance with the descriptions he has given. The question, however, raised by my researches, is whether unwarranted conclusions have not been drawn from them through a source of fallacy having been overlooked.

For example, in Bernard's experiment the life of an animal that had been previously kept upon food devoid of starch and sugar was destroyed, and blood collected in an ordinary manner from certain parts of the circulatory system. It was found upon examination that the blood escaping from the liver was pretty abundantly charged with sugar, whilst that flowing to the organ was free, or, speaking more precisely, next to free from it. The liver also, unlike the other organs and textures of the body, was found to contain a large quantity of sugar. Now, it is to be observed that these results, looked at strictly, only furnish evidence of the condition actually existing *after death*, but they have been taken as representing the *ante-mortem* or *physiological* state. Although it would hardly be thought that any error could have arisen out of this circumstance, seeing that so short a space of time elapsed before the examinations were undertaken; yet it remains to be seen whether such, in reality, does but happen to have been the case. It remains, in other words, to be seen whether a different mode of experimenting does not show that the theory of glycogenesis has been raised upon a fallacious foundation.

From the old method of experimenting it had been inferred that a destruction of sugar took place in the lungs. Blood had been collected from the arterial system during life, and found to contain only a trace, or but little more, of sugar. The animal had then been killed and blood collected from the right side of the heart, and in this, sugar in quantity was found to be present. Now, whilst prosecuting some researches on the presumed destruction of sugar in the lungs, I unexpectedly came across the fact that the state of the blood belonging to the right side of the heart during life was not correctly represented by the mode of procedure that had been hitherto adopted. The *ante-mortem* and *post-mortem* states, in other words, do not correspond. What, it must be admitted, we want for physiology is a representation of the condition existing during life, and this, it happens, we fail to obtain in the case in point unless we operate upon blood, cardiac as well as arterial, that has been collected before or at the very *instant* of death.

In the researches referred to on the presumed destruction of sugar in the lungs, I was experimenting to see if the sugar could be made to disappear by injecting the blood through the artificially inflated lungs of a recently killed animal. The blood was at first collected from the right side of the heart after death, and employed before coagulation had taken place. Finding in these experiments that the process of coagulation interfered with the satisfactory performance of the injection, I looked for an improved method of procedure, and tried the effect of using blood obtained by withdrawal during life, by means of a catheter introduced into the right ventricle. Such an operation can be readily performed, and without giving rise to any appreciable distress or disturbance.

Now, upon examining the blood obtained in this way I found that it presented quite a different behaviour, in respect of sugar, from what I had been led to look for. I noticed, instead of its giving a strong reaction, such as I had hitherto been accustomed to meet with in the case of blood collected from the right side of the heart *after death*, that it yielded only a very slight one—just such a reaction, indeed, as had been recognised as obtainable from the blood contained in the arterial system.

To this observation I did not at first attach the importance that was due to it. Subsequently, however, returning to the subject, and again encountering the same result, I began to see that something really existed which required to be cleared up. At first I was so strongly impressed with the notion that the glycogenic doctrine was indisputably established—so thoroughly satisfied, in accordance with the prevailing opinion, that sugar was extensively formed by the liver during life, and poured into the circulation through the hepatic veins—that I was for some time disposed to believe there must be a fallacy of some kind or other connected with my experiment to account for what I had noticed. I felt inclined to think that the catheter had not been fairly introduced into the heart, or that it had come in contact with the current of blood descending through the superior cava, rather than dispute the accredited doctrine, and no longer regard the strongly saccharine state of the blood encountered after death as a representation of its natural or *ante-mortem* condition.

Misgivings, however, soon began to occupy my mind, and the desirability of undertaking an attempt to clear up the discrepancy forced itself strongly upon me. From numerous experiments, performed with the greatest care, I learnt that there was no source of fallacy where fallacy, I had thought, might exist. It became evident now, that what had hitherto been regarded as the natural or physiological state of the blood of the right side of the heart was not in reality such. Blood, I found, that had been removed from this part of the circulatory system during life did not behave like that collected, as had hitherto been the custom, after death. Whilst that collected after death gave rise to the production of a copious orange-yellow or orange-red deposit of reduced oxide with the cupro-potassic solution, that obtained during life gave only a very slight sign of reaction—no more, in fact, than had hitherto been recognised as yielded by the blood belonging to the arterial and likewise the general venous system.

To prove that I had operated upon animals where there had been no want of power to produce sugar, I made a quantitative analysis of the blood collected from the heart in an ordinary manner after death and likewise of the liver, after noting that the blood collected during life gave only the traceable reaction of sugar that I have referred to. In five experiments conducted upon dogs, the following are the results that were obtained:

	Blood from the carotid artery and the right ventricle during life.	Blood from the right side of the heart after death. Sugar, per cent.	Liver a short time after death. Sugar, per cent.
No. 1.	Trace of sugar.	$\frac{7}{10}$ gr.	Not analysed.
2.	„ „	$\frac{65}{100}$ „	4·10 grs.
3.	„ „	$\frac{5}{10}$ „	3·39 „
4.	„ „	$\frac{94}{100}$ „	2·45 „
5.	„ „	$\frac{7}{10}$ „	2·44 „

I had not, as yet, tried to determine the actual amount of sugar existing during life in right-ventricular blood, but I now proceeded to do so. A known quantity of defibrinated blood was poured into spirit, and the precipitate separated by filtration and thoroughly washed to remove all the sugar. The whole of the liquid was then evaporated to a small bulk, and the sugar estimated with the cupro-potassic solution. In three instances I found the amounts indicated to be respectively forty-seven, fifty-eight, and seventy-three thousandths of a grain per cent. These results may be taken as affording an average representation of the amount of sugar normally present; for the specimens were tested in an ordinary manner with the copper solution, and found to give the same kind of behaviour as the numerous other specimens that I had examined in the same way. In the case of the first two of the analyses the blood was taken within a few hours after the animals had been fed; in the third twenty-four hours had elapsed after food had been administered.

To obtain a perfectly natural specimen of blood for examination, it is necessary that the animal should remain in as complete a state of tranquillity as possible during the performance of the operation required for its removal. Very slight causes are sufficient to lead to the appearance of a considerable amount of sugar in the blood throughout all parts of the system. It is surprising how rapidly the effects of muscular efforts of resistance, and embarrassment of the breathing, become manifest. According to the state of the animal during the removal of the blood, the kind of reaction that will be obtained, as regards sugar, can be predicated with confidence. To obtain a representation of the natural state, natural circumstances must prevail at the time of collection. Should there be either any violent muscular action in the form of efforts of resistance or embarrassment of the breathing, an extensive indication of the presence of sugar will be sure to be met with. Indeed, as I shall show further on, by simply interfering with the due performance of the respiration I have caused such an amount of sugar to make its appearance in the circulation as to lead, in the course of a very short time, to a strongly saccharine state of the urine being induced. By the adoption of measures, for instance, to reduce the supply of air to a point just short of producing asphyxia, I have succeeded in rendering the urine, in an hour's time, strongly saccharine.

The appearance of sugar in the circulation that takes place under these circumstances is, I believe, to be accounted for in the following manner. During violent muscular efforts the liver will be subjected to mechanical compression by the contraction of the muscles belonging to the abdominal parietes. By obstructing the breathing the circulation of the blood through the lungs is impeded, and general venous congestion induced. Now, we have here conditions that must tend to bring the amyloid substance existing in the liver-cells, and the blood contained in the blood-vessels, into unnatural relation to each other, and any admixture of amyloid substance with the blood will immediately give rise to the production of sugar. These, however, are points that I shall specially have to advert to in a subsequent part of this work.

The circumstances I have just been alluding to afford an explanation of why the blood removed from the carotid artery immediately after the exposure of the vessel may be found (as is often the case) in a marked degree more saccharine than when collected after ten minutes or so have been allowed to elapse. From the contiguity of the carotid artery to the pneumogastric nerve, picking up the vessel is almost sure to produce strong muscular efforts and considerable disturbance of the breathing. When the artery, however, has been once fairly exposed and separated from its adjacent structures, and a ligature placed around it, it can be easily drawn out and blood collected from it without occasioning any fresh muscular efforts or respiratory disturbance.

Upon a few occasions I found blood removed from the carotid artery giving a shade stronger reaction than a specimen previously withdrawn by the aid of a catheter from the right side of the heart. This I have looked upon as dependent upon the difference in the nature of the operations respectively required to be performed for procuring the blood. The operation of exposing the jugular vein, and passing a catheter through it into the heart, is not so likely to produce resistance and disturbance as exposing the carotid artery, which is much more deeply situated in the neck, besides lying in proximity with the pneumogastric nerve.

The administration of chloroform must also be avoided when a specimen of blood is sought for in a natural state as regards sugar. Chloroform not only reacts of itself with the copper solution, but, through its influence on the system, determines (as I shall show further on) an unnatural appearance of sugar in the circulation.

With the knowledge that is now possessed of the precautions to be taken, it is easy to operate in such a manner as to alight upon the blood after death in the condition that naturally belongs to it during life. Should an animal be killed, and even a short time only be allowed to elapse before the chest is opened to collect the blood from the right side of the heart, a strongly saccharine reaction will be encountered. If, however, after the instantaneous destruction of life the chest is as rapidly as possible opened, and the heart quickly ligatured at its base and excised, then the blood contained in its right cavities will be found as free from sugar as if it had been obtained by catheterism performed under a tranquil state during life. Here the steps of the operation are so rapidly carried out that time is not given for any *post-mortem* effects to be exerted upon the blood.

I think, indeed, that this is the best mode of proceeding to obtain a representation of the natural state of right-ventricular blood. When the experiment is expeditiously and properly performed the result is not exposed to the chance of being vitiated by the operation of any accidental disturbing influences ; and thus, it may be considered as forming a more certain method of procedure than catheterism of the right ventricle during life. The reason of the experiment requiring to be so expeditiously performed will fully appear when it is taken into consideration with what surprising rapidity (as will presently be shown) sugar is formed in the liver after death. By the continuance of the circulation, which occurs for a minute or two after the destruction of life by pithing, the ordinary mode of destroying life adopted by the physiologist, the sugar that is thus formed is carried to the right side of the heart, and thence into the arterial system through the lungs.

It has been stated that, when the requisite precautions are taken to obtain a representation of the physiological state of the blood derived from the right side of the heart, it is not discovered to be appreciably more saccharine than that derived from the arteries and veins. Now, the same may also be said of the right-ventricular blood as compared with that of the portal vein, taking for experiment an animal feeder. In three successive experiments upon dogs, I carefully compared the blood from the right side of the heart with that collected from the portal vein. The specimens were treated as closely alike as it was possible to do; and, when tested with the cupro-potassic solution, the portal blood yielded the same slight reaction that was given by that derived from the heart. It was impossible, in fact, by means of the reagent, to recognise any appreciable difference in either of the experiments between the two. Now, one of the principal arguments upon which the glycogenic theory has been founded is, that a striking difference exists in the blood that has escaped from the liver, as compared with that which is flowing to it—the one, it was said, being highly charged with, the other free from, sugar. It seems, however, that no such difference, taking the blood in the condition belonging to life, in reality can be traced.

As far, then, as we learn from what has preceded, there is not, as a natural process of life, that flow of sugar into the circulation from the liver, for the purpose of destruction in the lungs, which the former mode of experimenting led physiologists to believe existed. After death, and under certain unnatural states during life, it is true there is a large escape of sugar from the liver; but, as a normal condition, there is only a trace of sugar to be encountered in the blood between the liver and the lungs,—the same, in fact, that is also to be met with on the other side of the lungs; in the blood returning from the system at large; and even in the blood that is flowing towards the liver. The blood, therefore (viz. that escaping from the liver), which was formerly looked upon as affording the evidence upon which the glycogenic theory was founded, has nothing special belonging to it. As nearly as possible the same behaviour, as far as I can discover by the closest examination, is presented, no matter from what part of the circulatory system the specimen of blood may have been derived.

Quitting, now, the subject of the state of the blood, let me next direct attention to that of the organ itself which has been reputed to enjoy the glycogenic function.

After discovering the fallacy of taking the condition of the blood collected in an ordinary manner from the right ventricle after death, as a representation of its natural or physiological state, I still regarded the liver as standing in the same position as before. It did not at the commencement occur to me that a similar fallacy might here also prevail; and I first undertook some experiments consisting of injecting blood through the liver at different pressures, with a view of ascertaining if I could in this way discover the reason of the escape of sugar from the organ after death, and its non-escape during life. Failing, however, to meet with anything satisfactory, I began to think that possibly the liver, like the blood flowing from it, might not be in the saccharine state *during life* that had been inferred from previously conducted *post-mortem* examinations. Without the slightest anticipation of finding such to be the case, I instituted some experiments directed towards coming down upon the state of the organ in relation to sugar, as it were, nearer to that of life than had hitherto been done. This I sought to accomplish by suddenly placing it in a condition to arrest any change that might be attended with the production of sugar in the act of, or subsequently to the occurrence of, death.

Knowing I had a material to deal with, existing in the liver, which passed with great rapidity into sugar, under the influence of ferments, I looked for an agent possessing the power of preventing this transformation, without destroying the material or its product. Experiments were conducted with a solution of amyloid substance, apart from the liver, making use of saliva as a ferment. Various agents were tried, to see if I could find something to prevent the saccharine metamorphosis taking place, without effecting the destruction of the bodies concerned. The alkalies were found to answer the purpose. A very small quantity of potash, added to a solution of amyloid substance, sufficed to prevent the operation of saliva as a transformative agent. Upon discovering this fact I was led to perform the experiment of injecting the liver with potash. The alkali having been found to prevent the action of saliva as a ferment, I inferred that it would probably exercise a similar influence upon other ferments; and thus I thought that on injecting a strong solution of it through the portal vein into the liver as expeditiously after the destruction of life as practicable, I should meet with a representation of the state of things, as far as amyloid substance and sugar were concerned, actually existing during life; or, if not this, with a representation that could not be very far removed from it.

Upon the injection of potash into the liver being carried out in the manner I had proposed to myself, to my astonishment I failed to recognise the accustomed behaviour of the organ as regards sugar. There was now only a mere trace of sugar to be discovered upon examining the substance of the liver, in the place of the copious reaction that I had hitherto been accustomed to encounter. That the potash had not destroyed the sugar, but simply prevented its production, was shown by injecting a liver that had been allowed to remain unoperated upon a short time after death, to permit the formation of sugar to take place. Now, the result, under these circumstances, was that the presence of sugar was as readily to be displayed as if the alkali had not been used. A saccharine liver injected with potash gives as strong a reaction of sugar, after being treated in the appropriate manner for testing, as if the injection had not been practised.

By means of a modification in the mode of experimenting, it was shown that no objection could be raised to the result of my experiment by presuming that the liver employed was not in a healthy state, and would not have given, had it been left to itself, a saccharine reaction. Instead of potash being thrown into the whole of the liver, a portion was held so as to prevent the injection flowing into it. Thus, two specimens were obtained; and, on being tested, the one which had not been penetrated by the alkali gave a strong reaction of sugar, whilst the other, as in the previous experiments, yielded next to none.

Some time later I learnt that the *carbonated* exerted the same effect in preventing the production of sugar as the *caustic* alkali, and this even when used in moderate quantity. In one experiment 200 grs. of the carbonate of soda, dissolved in an ounce of water, were injected into the liver of a dog, through the portal vein, instantly after the destruction of life by pithing, and found to suffice for the purpose. A couple of lobes happened to escape being properly penetrated by the injection, and in this portion of the liver the ordinary *post-mortem* production of sugar, as was shown by the reaction it presented, ensued. In the other portion, however, an absence of sugar was observed on being tested shortly after the injection, and even when examined again on the following day.

Acids are also endowed with the power of checking the action of ferments upon the amyloid substance of the liver. And hence, with the injection of a strong solution of citric acid, I have obtained the same result as with the injection of a solution of potash.

In all these experiments, as may naturally be supposed from what has been mentioned, everything depends upon the promptitude with which the injection is effected after the life of the animal has been destroyed. The transformation of the amyloid substance into sugar takes place with such rapidity after death that, unless as little loss of time as possible is allowed to occur, an unsuccessful result is sure to be obtained.

From the information supplied by these experiments I now saw the explanation of what I had noticed and had puzzled me so much with regard to the state of the blood before and after death. I had no longer to look for conditions that prevented sugar from passing from the liver into the blood-vessels during life. Sugar did not pass, because it did not exist, not being produced in the liver during life as it is after death.

Although I believe that the mode of experimenting that has been referred to may be taken as affording reliable evidence as to the physiological state of the liver in relation to sugar, yet there is another and a simpler process by which the organ may be alighted upon in the condition belonging to life. Results obtained with the assistance of strong chemical agents, like acids and alkalies, might be looked upon with suspicion by some; but those in which the agency of temperature only is brought into play, cannot, I think, be likely to be open to any objection. Now, it happens that, by exposing the liver instantly after death to the influence of either boiling or freezing, the effect that is wanted may be produced. Freezing suspends organic chemical changes; and boiling destroys the activity of the ferment by which the metamorphosis is effected. By neither of these agencies can any destructive influence be exerted on the amyloid substance or sugar.

For the application of freezing, a mixture of ice and salt is employed. The mixture should be allowed to partially liquefy before being used, as its power of rapidly abstracting heat is thereby much enhanced. The object to be attained is to reduce the temperature as quickly as practicable to a degree at which the ferment ceases to possess activity. The life of the animal being destroyed by some sudden process, as by pithing, the abdomen must be instantly opened, and a piece of liver quickly excised and plunged into the freezing mixture, in which it should be stirred about. In the course of a few moments the specimen of liver that has been thus treated will be found to be frozen quite hard. It is now to be taken and cut into slices, reduced to a pulp in a mortar, and introduced, a little at a time, into a small quantity of boiling water, contained in a porcelain capsule, heat being applied so as to keep the contents of the capsule briskly boiling all the while.

The necessity of closely following the particular method of procedure indicated for procuring a decoction of the frozen liver for testing will be apparent when it is taken into consideration that the amyloid substance and ferment are both present in an unchanged state in the specimen, and that by a *gradual* elevation of temperature an opportunity would be given for some amount of transformation to occur. As it was necessary to reduce the temperature as rapidly as possible during the process of freezing, so it is likewise necessary to raise it suddenly in procuring the docoction, in order to prevent the result being vitiated by allowing sugar to be formed during the preparation of a liquid for testing.

The decoction of liver thus obtained is highly milky, from the abundance of amyloid substance that it contains. On being tested with the cupro-potassic solution, it will be found to give no indication, or, at the most, only a traceable indication, of the presence of sugar.

The portion of liver left behind, and not submitted to the influence of freezing, but treated in the manner it was formerly the custom to do, will be found to give rise to a more or less copious reaction on being tested with the copper solution.

It is easy to show that only a suspension of change has been effected by the process that has been employed; for, if a piece of the frozen liver be exposed for a short time to a temperature of about 90° or 100° Fahr., an abundance of sugar will be found to be present.

I need hardly say that a specimen of liver which has become saccharine after death loses none of its saccharine quality by being immersed in a freezing mixture.

I have found the rabbit to constitute a more suitable animal for this experiment than the dog. It is altogether of a more manageable nature, which allows the steps of the operation to be more quickly carried out. The liver, also, being thinner, is more speedily penetrated throughout by the cold. With a thick piece of liver, indeed, I have before now noticed that, when the outside portion has been frozen quite hard, and found devoid of sugar, the central portion has still been soft, and found to yield a moderate reaction. It is obvious that, with a thick mass of liver, greater time must be required for the influence of the freezing mixture to penetrate to the centre than with a thinner specimen. Whether the animal be taken during the performance of digestion or not, makes no difference, as far as I have perceived, in the result. As a rule, my experiments have been conducted a few hours after the administration of food.

An equally satisfactory result is obtainable by the aid of boiling water as by the freezing mixture. The principles that are capable of acting as ferments are coagulated by exposure to a boiling heat, and so rendered inert. In the absence of an active ferment there is no transformation of amyloid substance into sugar.

For the application of this process, a piece of liver that has been removed from an animal instantly after being suddenly killed is plunged into a quantity, say about a quart, of water that has been previously made to briskly boil. The specimen of liver taken should not be too large, or too thick, in order that it may be rapidly penetrated throughout by the heat. A few incisions into it facilitate the penetration and so render the effect more complete. A minute or two's immersion will suffice for producing what is wanted, and all that is necessary in preparing a liquid for testing is to pound in a mortar, add a little water, boil in a capsule, and filter. The decoction of liver thus obtained, should the experiment have been properly conducted, will only give the faintest indication of the presence of sugar.

In accordance with what has been previously stated, it will be readily understood that with every degree of increase in the elevation of temperature, short of the point at which the ferment loses its activity, the condition becomes more and more favorable for rapidity of transformation of amyloid substance into sugar. Hence, unless the destruction of the ferment is quickly effected an unsuccessful result cannot fail to be obtained. Looking at the rapidity with which the production of sugar occurs at an elevated temperature after death, and the fact that a certain space of time, however dexterously the experiment may be performed, must necessarily elapse before the ferment is destroyed, the presence of a trace of sugar in the decoction examined can be satisfactorily accounted for without falling back upon the presumption of its existence during life.

In the case of a cold-blooded animal the circumstances permit a representation of the natural or living condition of the liver to be readily obtained without resorting to the special expedients that have been mentioned. The temperature of the body of a cold-blooded animal varies with that of the medium which surrounds it, and thus a very much lower temperature, even under ordinary circumstances, prevails at the time of death than in the warm-blooded animal. Now, the influence exerted by temperature on the *post-mortem* transformation of amyloid substance has just been pointed out; and, from what has been said, it follows that, during cold, or moderately cold, weather, or after exposure of the body artificially to cold, the liver of a cold-blooded animal will be readily susceptible of being alighted upon in the state that belongs to life.

It happens that the frog forms an exceedingly convenient animal for this, as for so many other physiological experiments. It did not escape the notice of Bernard that the liver of this animal was to be found in a saccharine condition or not, according to the temperature existing at the time of death. In the 'Comptes Rendus' of the Academy of Sciences, March, 1857, he states that by lowering the temperature of frogs a disappearance of sugar may be made to take place from the liver, and that by afterwards exposing them to heat it is found to reappear. He adds that it is possible to produce this singular alternation of appearance and disappearance of sugar several times, without any food being given, by acting solely on the circulation through the medium of temperature. It may be stated that the idea he entertained regarding the cause of the phenomenon was that it depended upon an alteration in the activity of the glycogenic function, brought about by an increase or decrease in the activity of the circulation, as the result of the alteration of temperature.

Whilst experimenting myself upon frogs, I obtained results corresponding with those of Bernard, without being aware that his experiments had been conducted. Frogs, in good condition, where the livers were found large, pale coloured, and exceedingly rich in amyloid substance, were exposed for a couple of hours to the influence of an atmosphere heated to a temperature of 90° Fahr. An examination of the livers made in the ordinary way furnished decided evidence of the presence of sugar. The livers of similar frogs, on the other hand, that had not been similarly exposed, gave no reaction on being tested for sugar.

Whilst repeating these experiments, I one day met with a result for which, at the time, I could not satisfactorily account. Some frogs that had been exposed to a heated atmosphere happened to be removed and placed aside for about a quarter of an hour before being killed and examined. The livers yielded a scarcely appreciable indication of the presence of sugar. With the knowledge that we now possess it is easy to see the cause of this result. By the delay that had occurred before the frogs were killed and examined, time had been given for the temperature of the body to fall more or less completely down to a level with that of the surrounding air. Now, the influence that temperature exerts upon the *post-mortem* transformation of amyloid substance into sugar has been fully considered, and, from what has been said, it will be seen that upon this will depend the state in which the liver is found after an ordinarily conducted examination, such as used to be practised.

The oyster and mussel I have found answer equally as well as the frog for displaying the state of the liver belonging to life. In both of them the liver is charged with a large quantity of amyloid substance, but is easily shown to be entirely devoid of sugar when the animal is taken for examination in a fresh and healthy condition. Should the animal, however, have been allowed to die in a gradual way, or have been kept for some time out of water, and thereby thrown into an unhealthy condition, then sugar will be discoverable in abundance. An abundance of sugar is also to be encountered when the livers are removed and moderately heated for a short time before the examination is made.

In the mussel *(Mytilus edulis)*, not only does amyloid substance exist in the liver, but the mantle is also richly charged with it under a good-conditioned state of the animal. When the animal is poor, as after spawning, the mantle is thin, transparent, watery, and contains but little amyloid substance. Under an opposite condition, however, the mantle is thick, and opaquely white or yellowish, and in this state is highly charged with amyloid substance, which, therefore, seems to form a kind of store to be drawn upon during the season of spawning. No sugar can be detected in the mantle at the time of death, and, what is more, there is scarcely any disposition to the production of sugar after death, unless a ferment such as saliva be added, when the formation of sugar is freely observed to take place.

In a warm-blooded animal it is possible to lower the temperature previous to death, and thereby place the liver in a condition in which the state belonging to life may be as easily alighted upon as it is in the case of the frog, oyster, &c.

After the division of the spinal cord as high up as is consistent with the continuance of life—that is, just below the origin of the phrenics—the temperature of the body rapidly falls, if the animal is exposed to a moderate amount of cold. Now, Bernard noticed under these circumstances that the liver was to be found devoid of sugar when examined immediately after death, and that it became strongly saccharine afterwards. He endeavoured to account for the phenomenon under his glycogenic theory, but the various reasons he assigned show the difficulty he was under in giving a satisfactory explanation.

I have myself witnessed the phenomenon that has been referred to. It fully tallies with the several other results that I have been describing, and receives from them a ready explanation. The reduced temperature existing at the time of death diminishes the rapidity of the *post-mortem* transformation of amyloid substance into sugar, and so enables the process to be seen in a clear light as constituting an after-death event. As evidence of the extent of reduction of temperature that may thus be produced I may state that upon one occasion, in three hours and a half's time after the spinal cord of a rabbit had been divided, the temperature of the rectum was observed to stand at 67° Fahr., the animal still being just alive. This constitutes about the extreme point to which the temperature can be lowered before the actual occurrence of death.

Should the temperature be maintained by exposure of the animal to artificial warmth after the division of the cord has been effected, no deviation from the ordinary state of things is to be observed. Thus, a rabbit in which the spinal cord had been divided just below the phrenics was placed in an atmosphere heated to 88° Fahr. In three hours' time, when life was destroyed, a thermometer introduced into the rectum showed a temperature of 104° Fahr., which constitutes the temperature existing under natural conditions. The liver of this rabbit behaved precisely as if the animal had been suddenly killed, without any previous operation being performed upon it: that is, sugar was found in abundance after an ordinarily conducted examination. No reduction of temperature having been permitted to take place, there was the same rapid production of sugar after death that occurs under ordinary circumstances in the warm-blooded animal.

By oiling the coat of an animal, and so favouring the rapid escape of heat from the body, the temperature may be lowered, and the same effect produced as by division of the spinal cord. Placed in a warm situation, a rabbit will survive the operation; but exposed to cold, the radiation of heat, from the non-conducting properties of the coat having been destroyed, is greater than the capacity that exists for its production; and thus the temperature more or less rapidly declines, until a point is reached which is inconsistent with the further continuance of life. As soon as the temperature has arrived at about 65° Fahr. death is found to occur. Now, on destroying the life of the animal before a moribund condition has been produced, that is, when the temperature has descended, say, to between 70° and 80°, the liver is easily alighted upon in a non-saccharine state and found to become strongly saccharine afterwards.

Such are the facts that became gradually and unexpectedly disclosed by the prosecution of experimental research commenced with quite a different end in view from that which was arrived at. Originally a strong believer in, and supporter of, the glycogenic doctrine, I was compulsorily led by the unlooked-for evidence that presented itself to stand forward as an opponent to it.

Taking a review of the results that have as yet been brought forward, the position of the matter may be said to stand thus: the evidence upon which the liver was supposed to enjoy a sugar-forming function was based upon conditions met with after death. Now, it happens to turn out that these conditions can be shown to differ from those existing during life; and hence we are no longer justified in using them for the purpose they have hitherto been applied to, viz. as a foundation for conclusions regarding the physiological state. It is not that there is anything incorrect about Bernard's experimental results, as far as the results themselves are concerned, but what I have to speak against is that inferences have been drawn from them which they do not, strictly speaking, warrant. The results I have been describing as having been obtained by myself are perfectly compatible, not with our former conclusions, it is true, but with the experiments from which those conclusions were drawn. From an ordinary examination of the liver, and of the blood of the right side of the heart after death, we obtain reactions indicative of the presence of a large quantity of sugar, and the deduction hitherto drawn has been that the sugar existed there as a natural condition of life. Such a deduction, however, is obviously gratuitous. All that can be strictly or logically inferred from such an examination is that the liver and right-ventricular blood are in a saccharine condition *after death*. To obtain evidence of the state that exists *during life* requires a different mode of experimenting, and from such it appears that error has arisen through overstepping the strict letter of interpretation that the original experiments will bear.

The results that I have been describing have now been made known sufficiently long to afford an opportunity of being tested as to their accuracy by others, and it will here, perhaps, be desirable to pause and review what has been said regarding them.

It was in 1858 that the conclusions I had arrived at were communicated to the Royal Society in a paper entitled "On the alleged Sugar-Forming Function of the Liver," and about a year afterwards a discussion was raised by a communication from Dr. Harley concerning them. Dr. Harley had experimented, and, it appears, had failed in reproducing my results. He therefore contended that the glycogenic doctrine should be looked upon as still holding good. I was present at the meeting at which Dr. Harley's paper was read, and my answer was simply this—that I was prepared to stand by the statements I had made, and willing to undertake to verify them before any one that might desire to see the experiments performed. The experiments, it may be said, are of such a nature that a want of promptitude and dexterity in their performance will be inevitably followed by an unsuccessful result. No art is required to meet with sugar, for this is encountered when no precautions are taken. To obtain a non-saccharine behaviour the most prompt manipulation is absolutely indispensable in performing the experiment, and when this is exercised, according to my own experience, a successful result may with confidence be looked for. In opposition to the remarks of Dr. Harley, it can now be said that if he has failed, others in this country, and likewise on the Continent, have succeeded, as will be seen further on, in fully reproducing my results.

Dr. Thudicum, in "An Experimental Epicrisis of some late Researches on Liver Sugar" ('British Medical Journal,' March, 1860), opposed my conclusions on account of the method of procedure with potash, being open, as he considered, to objection. He imputed fallacy to the process from having been led, in reality (as I have pointed out in the 'Medical Times and Gazette,' April, 1865, where I have entered fully into a discussion of these objections and their refutation) into fallacy himself. But, besides this, his attack upon the potash process leaves the main question unaffected, as there are other means at disposal for arresting the *post-mortem* production of sugar without resorting to the use of potash. Indeed, it was only in my early experiments that the employment of potash was had recourse to, and it has long since been discarded, simpler and better means having been discovered for producing what is wanted.

Dr. M'Donnell, of Dublin, who has experimented largely upon the subject of glycogenesis, has discussed at length, in a brochure entitled "Observations on the Functions of the Liver," Dublin, 1865, the point under consideration.

As regards the blood, Dr. M'Donnell first of all states that he had become dexterous, from frequent performance of the operation, in obtaining right-ventricular blood by the use of the catheter from the living animal. In less than two minutes, with little struggling on the part of the animal, and but slight apparent injury to it, he could obtain between two and three ounces in quantity. "The blood thus obtained from the right side of the heart was treated with three or four times its bulk of proof-spirit, which was filtered off, the residue being repeatedly washed with additional spirit; the filtered spirit was evaporated to dryness on a water-bath, and the dry residue treated with distilled water was tested by Fehling's solution for the presence of sugar. The result was, that in twelve experiments made on dogs, which for some weeks before had been fed exclusively on meat, traces of sugar were found in five, and none in the remaining seven. None of these animals," he continues, "were killed at the time; but there is no reasonable doubt but that, as they were healthy animals, more or less of the amyloid substance existed in the livers of every one of them, and that, probably, the traces of sugar in the five were due to the dislodgment of some of it, in consequence of unavoidable struggling, and its transformation into sugar in the blood."

As regards the liver, he says—"In repeating Dr. Pavy's experiments on the tissue of the liver by freezing it, or boiling it, with the least possible loss of time after death, I have preferred to operate on cats rather than rabbits, because more or less sugar almost invariably pervades the tissues, or is discoverable in both the venous and arterial blood of these vegetable feeders." He supplies the following details of two experiments out of several, giving, he says, as nearly as possible similar results:

"A large, healthy cat, for some days before fed exclusively on flesh meat, was pithed three and a half hours after her last meal. At once a portion of the liver was cut off, and thrown into a quart of boiling distilled water. After being boiled for fifteen minutes it was taken out, weighed, and returned again to the same water. An equal weight (exactly 500 grains) of that portion of the liver which had remained in the animal was then (*i. e.* after a lapse of twenty minutes) likewise placed in a quart of cold distilled water and boiled. Each was boiled down to one-half. The portions of liver in each were bruised to a pulp; the boiling of each was then renewed; and, finally, each was evaporated to dryness on a water-bath. Each was treated with four ounces of proof-spirit, which was filtered off, and the residue washed with additional spirit. The spirit was evaporated on a water-bath, and the dry residues treated with equal quantities of distilled water, and filtered, so as to give a solution sufficiently clear for the application of the cupro-potassic test.

RESULT.

500 grains of liver, boiled immediately after death, gave an indication of sugar so slight as to be almost inappreciable, and incapable of being estimated.

500 grains of liver allowed to remain in the body of the animal for 20 minutes after death, contained 12·5 grains of glucose."

"A large, healthy male cat, for some days previously fed exclusively on meat, was pithed between three and four hours after his last meal. At once a portion of the liver was cut off and thrown into a capsule previously immersed in a freezing mixture of extreme coldness. This portion of the liver was immediately bruised with a pestle, already reduced to a very low temperature by immersion in the freezing mixture. In a very few seconds the whole was frozen quite hard on the sides and bottom of the capsule. It was then treated with two ounces of proof-spirit, which, after the lapse of two hours, was filtered off, and which passed through the filter almost perfectly clear. This, with the washings of the residue, was evaporated to dryness on a water-bath, and the residue treated with distilled water, so as to obtain a solution clear enough for the use of the cupro-potassic test."

"A portion of the liver which had been allowed to remain in the body of the animal for twenty minutes, and which, judging by the eye, was about the same size as that at once cut out and frozen, was bruised up with two ounces of proof-spirit, which, being filtered off, was evaporated to dryness, and the residue heated with distilled water, so as to obtain a solution suitable for testing.

RESULT.

The portion of liver frozen immediately after death gave an indication of sugar barely perceptible.

The portion of liver allowed to remain 20 minutes in the body, contained 3·8 grains of glucose."

Dr. Mc Donnell continues :—" It appears, then, that these experiments give results very closely agreeing with those of Dr. Pavy; but there are others even more strongly corroborative of his views. Thus, if a healthy, well-fed hedgehog be gradually reduced in temperature, by having ice placed near it, until it becomes torpid, and the temperature then be further reduced, until, by degrees, the entire animal is slowly frozen into a solid mass, the liver then taken from the body and treated as above described does not give the slightest evidence of the existence of sugar. By this device it is possible, as it were, to steal so gently upon life, that at the moment of its departure the amount of cold is sufficiently great to prevent any of the amyloid substance (which is by no means wanting in the livers of these animals) being converted into sugar. The fact that no sugar is found when this experiment is carefully performed, is perhaps the most conclusive evidence which can be offered that during life and health the liver is not normally employed in effecting this transformation."

In the 'Journal de l'Anatomie et de la Physiologie,' edited by Robin, Paris, 1866, there is a communication on glycogenesis by Schiff, who has identified himself with the subject almost from the beginning. He says :—" Dans ces derniers temps MM. Meissner et Jaeger ont confirmé les resultats de Pavy et les ont même exprimés d'une manière encore plus absolue." Meissner and Jaeger conducted their experiments upon living animals. They excised a piece of liver, and, after cutting it up with scissors, immediately plunged it into boiling water. The decoction thus obtained was found to contain no sugar, whilst sugar was discoverable in another portion of the liver of the same animal when treated according to Bernard's method. They insist (quoting Schiff) upon the necessity of a number of precautions being taken, and especially that of cutting up the liver into small pieces before being plunged into the boiling water, so that the heat may immediately penetrate the whole thickness.

Schiff further on states that he himself, in conjunction with Dr. Herzen, had repeated my experiments upon dogs, cats, rabbits, and guinea-pigs. Adopting the process of taking a piece of the liver instantly after death, cutting it up, and plunging it into boiling water, he obtained, he says, decoctions completely devoid of sugar. He proved the absence of sugar by the various chemical tests. He also satisfied himself that his results were correct, by finding sugar in the other portion of the liver which was purposely treated in the ordinary way. He likewise collected the blood which escaped from the liver and the vena cava, and found this to be similarly free from sugar. The conclusion he arrived at from his experiments is that the amyloid substance is not transformed into sugar under physiological circumstances.

I will now pass to the examination of the subject under another point of view, and here I think it will be admitted that further evidence is supplied corroborative of that derivable from the experiments already related. Whilst prosecuting the researches I have been referring to, the fact became disclosed that one source of the amyloid substance contained in the liver could be shown to be starch and sugar ingested with the food. In the course of experimenting I found that the size of the liver was in a marked manner influenced by the nature of the food, and that the difference observable was chiefly, if not entirely, dependent on a difference in the amount of amyloid substance present. With dogs that had been fed upon a vegetable diet I noticed, first, that the liver was of enormous size as compared with what I had been accustomed to meet with under an animal diet; and, secondly, that it contained a very large quantity of amyloid substance.

The observations that follow upon dogs restricted to particular kinds of food were made with the special view of obtaining precise information with regard to the points just referred to. The animals were all, as far as could be judged, in a perfect state of health at the time of being killed and examined. The results are given, without any exclusion, just as they presented themselves, under their respective heads; and no selection was made in the animals taken, except such as was found necessary, from some of them refusing to take the vegetable food or sugar. The dogs were weighed just before death, and the liver immediately after. The weight of the liver does not include the contents of the gall-bladder. In most of the examples the observation was conducted a few hours after food had been administered.

DOGS FED UPON A DIET OF ANIMAL FOOD.

	Weight of animal.		Absolute weight of liver.	Relative weight of liver to animal.	Amount of amyloid substance in liver.
	lb.	oz.	oz.		Per cent.
No. 1	15	8	7¾	1 to 32	—
„ 2	12	0	7¼	1 to 26½	—
„ 3	11	14½	6⅛	1 to 31	8·29
„ 4	15	10	7¾	1 to 32	5·24
„ 5	11	0	6⅛	1 to 29	—
„ 6	11	15½	6½	1 to 29½	—
„ 7	15	5½	8¾	1 to 28	5·61
„ 8	24	4½	11¾	1 to 33	8·45
„ 9	14	9½	7⅛	1 to 32	4·88
„ 10	17	0	8⅞	1 to 30½	10·95
„ 11	9	8	7¼	1 to 21	6·94
Total	158	11½	85¼	1 to 30	

Thus, the total weight of eleven dogs kept for several days prior to death upon a strictly animal diet amounted to 158 lb. 11½ oz., and their livers to 85¼ oz. This gives to the liver a relative weight of 1 to 30—gives, in other words, just over half an ounce of liver for every pound the animals weighed.

On casting the eye through the list it will be seen that in no case is there any very material deviation from the average of the whole, except, perhaps, in No. 11, which consisted of a three-parts grown pup. Even here, however, where the highest proportionate weight of liver was obtained, it falls far short, as will presently be seen, of the average observed under a vegetable diet, and also, an animal diet with the addition of sugar.

In the instances in which the amount of amyloid substance is given the analyses were all conducted under precisely similar circumstances. As soon as the liver, which was removed immediately after death, had been weighed, a piece was taken and examined, allowing as little time as possible to transpire for the loss of amyloid substance from *post-mortem* transformation into sugar to occur. The average given by the results of the analyses that are mentioned amounts to 7·19 per cent.

It will be noticed that nothing is said about the amount of amyloid substance present in the case of some of the dogs, and for the following reasons. In No. 1 no analysis was made; in No. 2 the result was not introduced, because the liver had been left in the animal for two and a half hours before being taken for analysis. The amount of amyloid substance then yielded was 3·37 per cent. In No. 5 the liver was left in the animal for ten minutes, and not examined until two hours after this. The amount of amyloid substance then given was 3·51 per cent. In No. 6 a mishap occurred in conducting the analysis, which rendered its completion useless.

In the case of Nos. 7 and 8 dogs an extra amount of food was given, for the purpose of seeing if any effect would be produced upon the amount of amyloid substance to be encountered. No. 7 consumed, during the four days prior to death, double the quantity that the others had been allowed; No. 8 was supplied with as much food (tripe was the food that all of them were fed upon) as it would eat, and the quantity it devoured was something enormous. It will be observed, however, that in neither of these instances was there any noteworthy deviation from the average of the whole; indeed, in No. 7 the per-centage of amyloid substance stood below it.

DOGS FED UPON A DIET OF VEGETABLE FOOD.

The five following examples will serve to illustrate the effect of a vegetable diet on the liver. The dogs were kept for several days previous to death upon food consisting of barley-meal and potatoes, or, where this was refused, bread and potatoes. The following are the results that were yielded :

	Weight of animal.		Absolute weight of liver.	Relative weight of liver to animal.	Amount of amyloid substance in liver.
	lb.	oz.	oz.		Per cent.
No. 1 . .	17	8	19¼	1 to 14½	—
„ 2 . .	11	8	12½	1 to 14½	—
„ 3 . .	15	8	11¾	1 to 21	9·87
„ 4 . .	18	10	28	1 to 10½	25·30
„ 5 . .	17	5	12¼	1 to 22½	16·50
	80	7	83¾	1 to 15	

Comparing these results with the ones that have preceded, it is seen that, whilst the relative weight of liver to animal stood at 1 to 30 under an animal diet, it comes out under a vegetable diet at 1 to 15, or exactly double. Representing it in other words, the livers here rather more than equalled in ounces the number of pounds the animals weighed, instead of being in the proportion of only just over half an ounce to the pound, as after the diet of animal food.

As regards the amount of amyloid substance contained in these livers, no actual determination was made in the case of Nos. 1 and 2, but it was observed to be exceedingly high, as may be inferred from the fact that it was from the state of these livers that I was led to undertake the investigation now under consideration. I have introduced the result obtained in No. 3; but it ought to be stated that the analysis was not made till an hour and a half after death; the figures are therefore lower than they properly should be, or otherwise would have been. Still, including this amongst the three analyses given, the average furnished amounts to 17·23 per cent. against 7·19 per cent., the average obtained under a diet of animal food.

DOGS FED UPON A DIET OF ANIMAL FOOD WITH AN ADMIXTURE OF SUGAR.

The sugar employed for mixing with the food in these experiments was the ordinary brown or moist sugar that is used for domestic purposes. Various devices had to be resorted to to conceal its presence and get the animals to take it.

In No. 1 of the subjoined examples the dog was kept for eight days on a diet of animal food and sugar. At first one third of a pound of sugar was administered daily, but after three or four days the animal showed a disinclination for food, vomited, and had bilious diarrhœa. The quantity of sugar was reduced to a quarter of a pound daily; the dog now devoured voraciously all that was given to it. The urine collected from the bladder after death gave a strong reaction of sugar (grape sugar).

No. 2 was fed for nine days on animal food and a quarter of a pound of sugar per diem. It consumed its food well at first, but during the last few days some trouble was experienced in getting the full allowance of sugar taken. There was scarcely any urine to be procured from the bladder after death, but what there was gave no saccharine reaction.

No. 3 was kept for eight days upon the same allowance as No. 2. The urine, after death, gave a slight but unequivocal reaction of sugar.

No. 4 was fed for five days in the same manner as Nos. 2 and 3; the urine collected after death gave a strong reaction of sugar.

Submitting these dogs to examination in the same manner as the others, the following are the results that were yielded:

	Weight of animal.	Absolute weight of liver.	Relative weight of liver to animal.	Amount of amyloid substance in liver.
	lb. oz.	oz.		Per cent
No. 1 . .	10 3	12	1 to 13½	12·80
„ 2 . .	11 14	12¾	1 to 14½	17·55
„ 3 . .	17 11	10¾	1 to 26	12·33
„ 4 . .	12 0	13½	1 to 14	15·37
Total .	51 12	49	1 to 16½	

The total weight of these four dogs being 51 lb. 12 oz., and that of the livers 49 oz., we have just under an ounce of liver for every pound weight of dog. The exact relative weight of liver to animal is as 1 to 16½, which, it will be observed, accords very closely with what was presented under a vegetable diet.

A determination was made of the amount of amyloid substance in all four of the livers, and the results yielded furnish an average of 14·5 per cent. Under a purely animal diet the average obtained was only 7·19 per cent. Comparing these results, therefore, it appears that the per-centage of amyloid substance was as nearly as possible doubled by the sugar that was added to the animal food. The largest average proportion of amyloid substance furnished by the series of observations, taken altogether, was under the diet of vegetable food, where, it will be remembered, it amounted to 17·23 per cent.

The liver, besides being increased in size by the addition of sugar to the animal food, underwent a marked alteration in its physical condition. Under a purely animal diet the organ may be described as firm and fleshy, requiring considerable force to break it down between the fingers. Under the animal diet with sugar it was found to be so soft as to be readily susceptible of being crushed by very slight pressure. It looked swollen and flabby, and was of a pale colour. The bile contained in the gall-bladder, I noticed also, was much paler in colour than it is observed to be under a purely animal diet.

There was another circumstance that I observed on examining the animals that had taken the sugar, which I consider worthy of being mentioned. Peyer's patches and the solitary glands of the intestine, especially those of the cæcum, in each case presented a prominence and a vascularity that forcibly attracted my attention.

In the case of three of the dogs, as stated in the particulars, the urine became saccharine under the administration of the sugar; and it may be mentioned that, although cane sugar constituted the form of sugar ingested, it was grape sugar that was present in the urine.

I may now direct attention to the results I have obtained upon the rabbit with reference to the influence of food upon the state of the liver, and they will be found to be in perfect harmony with those that have just been mentioned as having been obtained upon the dog. In the first place, it may be stated that the better the condition of the animal, the larger the quantity of amyloid substance that the liver will be found to contain. The condition in which most of the rabbits procurable in London are found is not one in which it may be considered a fair representation is afforded of the state of the liver belonging to perfect health, for, according to my own experience, it is quite the exception not to find the organ more or less pervaded with entozoa. Subjoined, however, I give, for the sake of illustration, the results of the examination of four rabbits which had been fed in an ordinary way, and were, to all appearances, in excellent condition at the time of being killed.

RABBITS AFTER FEEDING IN AN ORDINARY WAY.

	Weight of animal.	Absolute weight of liver.	Relative weight of liver to animal.	Amount of amyloid substance in liver.
	lb. oz.	oz.		Per cent.
No. 1 . .	5 3	3⅜	1 to 24	7·5
„ 2 . .	3 15	2⅝	1 to 24	6·69
„ 3 . .	7 8	3⅜	1 to 33	3·16
„ 4 . .	5 11	3¼	1 to 28	12·59

There is one circumstance that it is necessary to take into account on inspecting these observations upon the rabbit by the side of those upon the dog. The influence of the large quantity of extraneous matter, under the form of contents of the alimentary canal, included in the weight of the rabbit, must not be left out of consideration on looking at the relation between the weight of the liver and that of the animal in the two. The alimentary canal of the rabbit is not only of great length, but the contents, especially of the stomach and the very capacious cæcum, are exceedingly voluminous. The stomach and intestine, in fact, with their contents, in two instances where I undertook an examination with reference to this point, were found to equal one fifth in one case and one fifth and a half in the other of the weight of the animal. In the dog the relative weight of the same parts, and their contents, is very much less. In a dog that had been kept upon a vegetable diet I found the alimentary canal and its contents to form about the one eighth of its weight, and in another that had been kept upon an animal diet, only the one tenth.

The liver of a rabbit to which starch and sugar had been administered in combination with the ordinary food yielded a much larger per-centage of amyloid substance than was given in either of the instances above. The animal was supplied with its ordinary food, and, in addition, $\frac{3}{4}$ oz. of cane sugar and $\frac{1}{2}$ oz. of starch were introduced into the stomach (in the same manner as in the experiments next in order to be referred to) daily for three days running. On the fourth day the animal was killed, and, although the liver was not analysed until the day after death, it was found then to contain 22·7 per cent. of amyloid substance.

By the two following experiments the clearest evidence is afforded illustrative of the effect producible upon the liver by the ingestion of starch and sugar, and corroborative of what has preceded. Rabbits were taken and fed on starch and sugar only, and, for the purpose of comparison, other rabbits were kept without any food at all. Nothing could be more simple than the conditions of such experiments, and the results may, I think, be looked upon as affording direct and unquestionable evidence that starch and sugar contribute to the production of amyloid substance in the liver.

In the first experiment a couple of full-grown rabbits, as nearly as possible resembling each other, were taken. One was kept fasting, whilst the other was fed daily for three days, through a gum-elastic tube passed down the œsophagus into the stomach, with 1 oz. starch and $\frac{3}{4}$ oz. of *grape* sugar, reduced to a semi-fluid state by admixture with water. On the fourth day both rabbits were killed and examined, when the following results were yielded :

	Weight of animal.	Weight of liver.	Relative weight of liver to animal.	Amount of amyloid substance in liver.
	lb. oz.	oz.		Per cent.
Rabbit fasting .	3 1	$1\frac{2}{5}$	1 to 35	1·3
Rabbit on starch and grape sugar .	3 4	$2\frac{1}{5}$	1 to 18	15·4

The second experiment was made upon two half-grown rabbits, likewise as nearly as possible resembling each other as regards condition and size. One, again, was kept fasting, whilst to the other was administered 1 oz. of starch and the same quantity of *cane* sugar daily for three days. On the fourth day the two rabbits were killed and examined, and subjoined are the results that were obtained :

	Weight of animal.	Weight of liver.	Relative weight of liver to animal.	Amount of amyloid substance in liver.
	lb. oz.	oz.		Per cent.
Rabbit fasting .	1 14	1	1 to 30	1·4
Rabbit on starch and cane sugar . .	1 $14\frac{3}{4}$	$2\frac{3}{8}$	1 to 13	16·9

The livers of the rabbits to which the starch and sugar had been administered were noticed to present the same deviation from the ordinary physical condition that was mentioned as having been observed after the administration of sugar to the dog. They were of a very pale colour, and so soft as to readily give way under the slightest pressure between the fingers. In one case, indeed, the liver was in so soft a state as to be almost pulpy, scarcely, in fact, holding together when taken up with a pair of forceps.

With such results to deal with, so confirmatory as they are of each other, both in the case of the rabbit and the dog, I do not see how any other conclusion can be arrived at than that sugar introduced into the alimentary canal from without is transformed into amyloid substance in the liver. It may be considered that we have here the first step in the assimilative process to which sugar is subjected in the animal economy.

It must not be inferred from what has preceded that sugar and starch form the only source of the amyloid substance encountered in the liver. It is quite certain, indeed, that it is not so; for, notwithstanding that saccharine and amylaceous materials have been altogether excluded from the food, amyloid substance is still discoverable in the liver. There is reason to believe that the liver is capable of forming amyloid substance out of the products of the retrograde metamorphosis of animal food introduced in excess into the system, as well as out of the products derived from the wear and tear of the tissues—materials, by such a process, being brought into a condition for further utilisation in the system, instead of being at once discharged as useless.

Under starvation and disease no amyloid substance is to be met with in the liver, and thus is accounted for the non-saccharine condition in which most of the livers derived from the *post-mortem* room are observed; for if no amyloid substance be contained in the organ at the time of death, no *post-mortem* production of sugar can occur.

As I have already remarked, I did not observe in my experiments upon dogs restricted to an animal diet, that increasing the amount of food beyond the ordinary allowance led to an increase in the size of the liver, or in the amount of amyloid substance that was present. Now, with reference to the influence of different kinds of food, nitrogenized included, upon the amount of amyloid substance contained in the liver, I have performed a further series of experiments upon rabbits, the results of which are shown in the statement below. The rabbits were kept for a few days prior to death exclusively upon the kind of food respectively mentioned, its introduction into the stomach being effected by means of injection through a gum elastic tube passed down the œsophagus into the organ.

Rabbits submitted for a few days prior to death to dieting upon various kinds of food, with a view of determining the influence produced upon the amount of amyloid substance contained in the liver.

Nature of food administered.	Amount of amyloid substance in the liver.
STARCH AND CANE SUGAR.	Per cent.
Starch, 1 oz.; sugar, 1 oz.	12·9
Do. do.	20·5
Do. do.	27·6
STARCH, SUGAR, AND ALBUMEN.	
Starch, 1 oz.; sugar, 1 oz.; white of 1 egg.	15·7
Do. do. whites of 2 eggs.	17·0

Nature of food administered.	Amount of amyloid substance in the liver.
STARCH, SUGAR, AND GELATINE.	Per cent.
Starch, ¾ oz.; sugar, ¾ oz.; isinglass, 25 grs.	14·1
Do. 1 oz.; do. 1 oz.; do. 30 grs.	10·4
Do. do. do.	12·0
STARCH, SUGAR, AND LIQ. POTASSÆ.	
Starch, 1 oz.; sugar, 1 oz.; liq. pot., ʒj.	17·7
STARCH, SUGAR, AND PHOSPHORIC ACID.	
Starch, 1 oz.; sugar, 1 oz.; ac. phos. dil. (Phar.), ʒj.	21·4
Do. do. do. ʒiss.	15·3
STARCH, SUGAR, AND ACETATE OF POTASH.	
Starch, 1 oz.; sugar, 1 oz.; acet. of potash, 40 grs.	13·1
Do. do. do.	19·0
Do. do. do. 60 grs.	17·6
STARCH, SUGAR, AND CITRATE OF POTASH.	
Starch, ½ oz.; sugar, 1 oz.; citrate of potash, 15 grs.	16·3
Do. 1 oz. do. do.	18·6
GUM.	
Gum arabic, 1½ oz.	10·9
Do.	4·8
OIL.	
Olive oil, ʒvj.	Trace.
Do.	None.
Do.	None.
GELATINE.	
Isinglass, 30 grs.	None.
Do. 150 grs.	Trace.
ALBUMEN.	
Whites of 2 eggs.	None.
Do. 4 eggs.	Trace.

On casting the eye through the above table, it will be seen that whenever starch and sugar were administered there was a good per-centage of amyloid substance present, no matter what the other principle administered also. The alkali, acid, and vegetable saline matter were administered to see if evidence would be afforded of the formation or destruction of amyloid substance being thereby influenced. Under gum there was some amyloid substance present; whilst under oil, gelatine, and albumen, there was none or only a trace.

Dr. McDonnell has also made some experiments upon this subject, and his results accord with my own. In his exhaustive little treatise (' Observations on the Functions of the Liver,' Dublin, 1865), he says—" It is surprising, and, indeed, almost incredible, to what a degree, and with what rapidity, the liver may be increased or diminished in bulk by the administration of particular kinds of diet. So far as this is due to an increased or diminished quantity of the amyloid substance stored up in the liver, the following table will show.

"*Average quantity of amyloid substance found in the entire liver of animals fed for some days on the following materials.*

	On a diet consisting almost entirely of starch and sugar.	On a diet of fat.	On diet of gluten bread.	On a diet of gelatine.
Dogs . . .	980 grs.	Hardly a trace	125 grs.	None.
Rats . . .	7 ,,	Ditto	3 ,,	None.
Pigeons . .	25½ ,,	—	1 ,,	—
Rabbits . .	45 ,,	—	8½ ,,	—."

The fact of amyloid substance being formed in the liver from sugar does not, of course, taken by itself, afford any direct evidence against the validity of the doctrine of glycogenesis; but this much may be said from it, viz. that for amyloid substance to be formed from sugar, with a view of being transformed back again into the same principle, certainly does not constitute a process that accords with the manner in which the operations of nature are ordinarily performed. Thus, indirectly do these results, showing that amyloid substance is derivable from sugar, tend to support the other evidence that has been adduced in opposition to the glycogenic theory.

I cannot conceive that it will be considered requisite to fall back upon a sugar-forming function in the liver to account for the trace of sugar naturally existing in the contents of the circulatory system. It may reasonably be referred to the occurrence of a mere chemical change arising out of the conditions that happen, as it were, incidentally to exist. The amyloid substance, in other words, happens to possess as one of its chemical properties a strong tendency to undergo transformation into sugar, a tendency which is more or less fully held in check, under natural circumstances, during life, but allowed to come into unopposed play after death. Now, to the existence of this tendency may be ascribed the trace of sugar met with in the circulation, without any physiological action being concerned, and also without its having any physiological purport.

It was suggested soon after my experimental results were first made known that, although the quantity of sugar found in the blood of the right side of the heart was extremely small, yet, supposing this small quantity to have come direct from the liver, and to be then at once destroyed, a fresh quantity taking its place, the amount formed in the twenty-four hours would constitute an item of considerable magnitude. Since we have become alive, however, to the errors attendant upon the old method of experimenting, and the fallacies to be avoided, it cannot be discovered that there is any destruction—certainly any appreciable amount of destruction—of sugar going on in any particular part of the circulatory system, as was formerly supposed. Sugar that may happen to reach the circulation circulates through it over and over again. It has been shown in a previous part of this work that the blood in the arterial system, as well as even that *flowing to the liver*, contains the same trace of sugar that is to be encountered in the contents of the right side of the heart. The details, it will be remembered, of some experiments upon animal-fed dogs were given, where a careful comparative examination of the blood from the right side of the heart and the portal vein was made, and it was found that there was no appreciable difference, as regards saccharine behaviour, to be discovered between the two.

There are other grounds still upon which the glycogenic theory has been considered to be open to attack, and the line of argument I am now about to refer to has originated in researches that have been conducted in Paris.

Bernard himself discovered that amyloid substance is to be met with in the placenta. By the reaction of the tincture of iodine, acidulated with acetic acid, and the aid of the microscope, its presence may be displayed as it is contained in the animal tissues. In rodents, by these means, he found it to be located in particular cells belonging to the placenta. In ruminants, strangely to remark, it is found in another situation. The placenta in these animals does not constitute a single compact organ, as in mammals generally, but consists of a large number of isolated masses, or placentulæ as they are called. Now, it happens that it is not in these placentulæ that the amyloid substance is to be found, but in patches of cells existing upon the inner surface of the amnion. To these patches, from the view he took of their office, Bernard gave the name of "plaques hépatiques." From the fact that the liver during early embryonic life contains no amyloid substance, and that the amyloid substance disappears from the above-mentioned situations before the end of utero-gestation, the placenta and the cell patches of the amnion were looked upon by Bernard as discharging a temporary glycogenic office—that is, fulfilling a function which he believed to be afterwards discharged by the liver.

This discovery of Bernard formed the starting-point for the investigations of Rouget, from which the fact was disclosed that amyloid substance not only exists in the appurtenances, as mentioned above, of the embryo, but is to be met with in several of the tissues of the embryo itself.

Rouget ('Journal de la Physiologie,' tome ii, Paris, 1859) was led to search for amyloid substance in the fœtus, from observing that the cells of the placenta and amnion which contained it were nothing else than epithelial cells. He at once found it in the epithelial cells of the alimentary mucous membrane, the genito-urinary passages, and the skin. It has also been found to exist largely in the growths from the skin, as hair, horn, hoof, &c., during their development in the embryo, but to disappear from these parts before birth. It has likewise been found to be present in cartilage during its earliest stage of development. The lungs, it appears, at one period, contain it in very large quantity; but as the end of utero-gestation is approached the quantity is materially diminished, and, in some instances, a total disappearance takes place. The muscles contain it even at birth, and for a short time afterwards, but in less proportion than it exists at an earlier period. As regards the liver, amyloid substance is not discoverable in it until its histological development is complete, or about the middle of intra-uterine life, after which it gradually increases in quantity.

Amyloid substance has also been encountered in the adult animal in certain situations besides in the liver. It is not ordinarily found in butcher's meat; but in animals that have been kept on food rich in starch and sugar the muscular tissue contains it. The flesh of horses, as shown by Sanson, is almost constantly impregnated with it. In ordinary well-fed mammals and birds it has been noticed to accumulate in muscles that are kept in a state of rest, and to disappear upon their being called into a state of functional activity. In hybernating animals it has been discovered both in muscular and lung tissue during hybernation, but is lost sight of in these textures when the animal is awake and active.

Now, seeing that the amyloid substance has been encountered so extensively as an animal product, the question naturally presents itself—if sugar formation be its purpose in the liver, is it not fair to presume that it will also be its purpose in the other situations where it is to be met with? and, if so, a sugar-forming function would have to be assigned to a variety of widely different organs and textures—that is, the muscles, the cells of the cutaneous, intestinal, respiratory, and genito-urinary surfaces of the fœtus, and the muscles and lungs of the adult, would have to be endowed with a glycogenic function. It has been argued, that instead of being destined for sugar formation, it is concerned, like fat and albumen, in the growth and development of the animal textures; or, like starch, in the growth and development of vegetable structures. The production of sugar, it has been urged, is not the object, but only the consequence, of the existence of amyloid substance, the phenomenon being due to a process of a downward change; just as the production of urea is due to a downward change occurring in nitrogenized substances.

Longet ('Traité de Physiologie,' Paris, 1861), says—"It is evident that, as regards glycogenesis, the liver of the adult is in the same condition as the embryonic organs, in the constitution of which amyloid substance enters. In the tissue of the liver, as in the embryonic tissues, during the progressive and retrograde changes taking place, amyloid substance is transformed into sugar; this latter being destroyed in the blood, or passing out in the urinary secretion, if formed in considerable amount." "The liver tissue," he continues, "is not the only one to present this speciality; for, under certain conditions, the muscular tissue, and also the lung tissue, contain amyloid substance and furnish sugar." Longet further thinks, with Rouget, that the transformation of amyloid substance into sugar does not constitute a special function of the liver, but simply results from the changes of nutrition going on in the organ.

Even upon these grounds only it was urged that sufficient evidence was afforded to deprive the liver of its reputed glycogenic function; and this, whilst the belief was still entertained, in accordance with the old method of experimenting, that sugar was contained in quantity in the organ and the blood escaping from it during life.

It has been shown, however, by my own researches, that sugar is not produced during life, as used to be believed, the sugar formerly encountered being, in reality, the result of a *post-mortem* change, instead of forming a representation of the natural or *ante-mortem* condition; and when this circumstance is taken into consideration, the argument adduced in Paris against the glycogenic theory will be seen to become, in an eminent degree, strengthened.

That there must be some other mode of transformation which amyloid substance is susceptible of undergoing in the liver besides into sugar is proved by what I will proceed to mention; for there are certain means, as will be seen, by which amyloid substance may be made to disappear, in an almost incredibly short space of time, without any sign of the production of sugar.

It has already been stated that under the existence of disease there is no amyloid substance discoverable in the liver. Now, I noticed, upon an occasion where 200 grains of carbonate of soda had been introduced into the stomach of a dog, and the animal had died in consequence in the course of a few hours, that the liver was found to be quite devoid of amyloid substance and sugar. This led me to undertake some experiments upon the injection of carbonate of soda into the portal system of the dog during life, and to these I will now direct attention.

In one experiment 60 grains of carbonate of soda were injected into a branch of the portal vein, and when the animal was killed, in from an hour and a half to two hours afterwards, no amyloid substance or sugar could be detected in the liver.

In another, 50 grains were injected, and the liver, examined in four hours' time, was found to be free from both amyloid substance and sugar.

In a third, the animal was killed an hour after 80 grains had been injected, and again the liver was found devoid of both amyloid substance and sugar.

In a fourth, the same result was met with after the employment of 200 grains, and likewise after the lapse of an hour.

Lastly, in two cases the liver, examined almost immediately, yielded no evidence of the presence of amyloid substance. In one of these cases 200 grains formed the quantity of carbonate of soda employed, and in this the liver was free from both amyloid substance and sugar; in the other, 100 grains were injected, and the liver was free from amyloid substance, but contained just a discoverable trace of sugar.

I learnt, in performing these experiments, that to get a disappearance of amyloid substance it was necessary that the liver should become swollen and congested as the result of the injection. When the injection was slowly made, and the blood allowed to flow freely through the vessels, the carbonate of soda seemed to pass through the liver, and to fail in producing a disappearance of amyloid substance from the organ. When, on the other hand, the carbonated alkali was rapidly introduced, it seemed, on arriving in the capillaries of the liver, to produce the effect of obstructing the flow of blood through the organ, and in this way to cause its passage being delayed. Obstructing the circulation, by interfering with the breathing, whilst the injection was being practised, I found also, assisted in bringing about the delay of the carbonate of soda in the liver and thus promoted its action in producing a disappearance of amyloid substance from the organ.

If, in these experiments, the disappearance of amyloid substance had been owing to its transformation into sugar, the sugar ought to have been readily susceptible of detection in the system; but the blood was found to present its usual behaviour—that is, to contain only just a trace of sugar. Calculating, indeed, from the average amount of amyloid substance contained in the liver of a medium-sized dog, subsisting upon an animal diet, at least from 150 to 200 grains of sugar would have to be accounted for. The supposition is not tenable that sugar was formed and immediately destroyed by the influence of the carbonate of soda, for it can be shown experimentally that the carbonate of soda has no such effect. In an experiment, for example, where 200 grains of grape sugar were injected into the portal circulation with 200 grains of the carbonate of soda, the blood throughout the system was found to be strongly charged with sugar, and the urine presented a strongly saccharine behaviour. Again, as showing that carbonate of soda does not occasion the destruction of sugar when once it has been formed, it was noticed, in one of the experiments where its injection was practised, that the urine was found, half an hour after its employment, from some cause or other that I could not explain, to be in a strongly saccharine condition, a proof that sugar must have existed in the blood. One hundred grains formed the quantity of carbonate of soda that was used for injection in this experiment.

In some experiments, where death has been produced by the influence of cold, I have noticed, also, a rapid disappearance of amyloid substance from the liver. I have before alluded to the effects of oiling the coat of an animal, and have there shown that in the case of the rabbit a marked lowering of the temperature can be in this way quickly induced. I then referred to these experiments to show that the *post-mortem* transformation of amyloid substance could, by such a method of procedure, be so retarded as to produce a condition in which the liver was susceptible of being easily alighted upon in the state belonging to life. Now, in some of the experiments that I have performed upon this subject a total disappearance of amyloid substance has been observed to take place, in the course of a few hours, from the liver. I have before me a record of five experiments where such a result was encountered. In one of them the rabbit was killed four and three quarter hours after the oiling of its coat; its temperature had fallen to 82° Fahr.; there was no amyloid substance or sugar discoverable in the liver. In a second the rabbit was killed four hours after the oiling, being then observed to be in a moribund condition; again there was no trace of amyloid substance or sugar to be discovered. In the third and fourth the rabbits died three and a quarter hours after the oiling; and in the fifth life was destroyed two hours after, the temperature of the body having then fallen to 70° Fahr. In each of these last three, as in the first two, there was no amyloid substance nor sugar to be found in the liver. I need scarcely say that all the animals were, as far as could be seen, in a healthy condition at the time of being taken for experiment, and hence it may be fairly inferred that the livers were charged to an ordinary extent with amyloid substance before the operation of oiling was practised.

I wish it to be understood that it is only in some and not in all of the experiments that I have performed that amyloid substance has been found to disappear from the liver, as was the case in those I have just referred to. In many of the experiments, for instance, that I have conducted, although the same conditions, as far as could be judged from external appearances, existed, the liver was found to be charged with a considerable quantity of amyloid substance, and this notwithstanding that life was maintained for an equal and even a longer period after the process of oiling had been performed. As a further illustration of the diversity that has been here encountered, I may state that upon two occasions I noticed, as an effect of the oiling and exposure to cold, a strongly saccharine condition of the urine.

Next comes the question—what constitutes the natural destination of the amyloid substance of the liver, if, as I contend is to be legitimately inferred from the array of evidence that has been brought forward, sugar formation does not? For my own part, I am induced to look in the direction of fat as forming the principle towards which the amyloid substance naturally proceeds. In the first place, it may be said that it has been ascertained beyond dispute that starch and sugar, introduced with the food, lead, in the animal system, to the production of fat. Now, it has been shown by what has preceded, that, from the ingestion of these principles, a striking increase is occasioned in the amount of amyloid substance contained in the liver. There can be no question, indeed, from the results that have been mentioned, that starch and sugar pass into amyloid substance in the liver. The production of amyloid substance, therefore, may be taken as representing the first step of assimilation of the starchy and saccharine elements of our food, and, as these elements are known to proceed on into fat, we have grounds for the surmise that amyloid substance simply occupies an intermediate position between the two. The process of assimilation may go on to the production of fat in the liver, or, it may be, that it stops short at the formation of another principle which escapes from the liver and is elsewhere transformed into fat. The resinoid matter of the bile, for instance, may be pointed to in reference to what I mean.

By Dr. M'Donnell the view has been propounded that the amyloid substance becomes united with nitrogen in the liver, and leaves the organ through the hepatic veins as a proteic compound; partly, perhaps, he thinks, under the form of globuline, and partly as a material in its reaction resembling caseine or albuminose. "May it not be," Dr. M'Donnell says, "that the liver does for the adult what divers tissues do during the development of the fœtus? May not this great organ form, with the help of the amyloid substance secreted in its cells, a nitrogenous compound, just as the muscles of the fœtus convert the amyloid substance contained in them into the highly nitrogenous materials of muscular tissue? May not, in fact, the amyloid substance of the liver be the basis of an azotized proto-plasma, forming a constituent of the blood of the adult animal, as the amyloid substance of muscle is the basis of the material from which the evolution of muscular tissue is accomplished?"

Another point that also forces itself upon us for consideration is this: Looking at the difference that has been pointed out as existing between the *ante-mortem* and *post-mortem* conditions of the liver and blood, how is it that the amyloid substance is not transformed into sugar during life, as it is immediately after death? The position that we have to deal with in reality stands thus:—Amyloid substance forms a constituent of the hepatic cells. Now, this amyloid substance happens to constitute a principle which possesses the chemical property of being exceedingly susceptible of undergoing transformation into sugar when brought into contact with certain bodies endowed with the power of acting as ferments. Such a body, I take it, as well as the amyloid substance, must be admitted as existing in the liver; but, whilst it is allowed to come into unopposed play after death, thereby leading to the production of the sugar that then occurs, it is held under control during life by some condition antagonistic to its activity. What this condition is forms an interesting and, it must be admitted also, a difficult problem for solution.

I may here remark that in the course of my experiments I have come across a few instances in which the usual *post-mortem* production of sugar has failed to take place in the liver, although amyloid substance has been contained in quantity in the organ.

One of these instances consisted of the liver of a cod fish, which, on being examined as soon as it fell into my hands, was found to be richly charged with amyloid substance, but to contain so slight an amount of sugar that the merest trace of reaction was given with the cupro-potassic solution. Examined again on the following day, the same behaviour was presented, and, what was more remarkable, a specimen of it exposed for three hours to a temperature of about 90° still only yielded evidence of containing a trace of sugar. The decoction of the liver was so strongly charged with amyloid substance as to be quite opaque, like milk; and by the addition of a ferment in the form of saliva, a copious production of sugar immediately took place.

A second instance consisted of the liver of an exceedingly healthy and good-conditioned rabbit, which had been fed on carrots shortly before the destruction of life. A decoction of the liver made in the ordinary way, a short time after death, although opaque, like milk, from the large amount of amyloid substance it contained, gave no reaction of sugar; and further, the liver, after exposure for several minutes to a moderately elevated temperature, gave evidence of only being charged with just a trace of sugar. Treating the decoction of the liver with a little saliva immediately gave rise to a large production of sugar.

A third instance consisted of the liver of a duck. The organ, although containing a large quantity of amyloid substance, only yielded, when taken for examination half an hour after death, a traceable indication of the presence of sugar.

The only way in which such results as these can be reconciled is by presuming that the usual ferment did not exist in the liver; or, what is less likely, that some condition prevailed to interfere with its manifestation of activity. Whatever may be the explanation, however, I am satisfied about the fact, for several examinations were made to secure that no error occurred in the performance of the analysis.

Schiff, I find, has noticed the same phenomenon. After stating that the livers of frogs during hybernation, although containing amyloid substance, do not become charged with sugar after death, as under ordinary circumstances, he remarks that he has observed an analogous state of things amongst warm-blooded animals. Three instances he remembers in which the liver contained amyloid substance, and in which, nevertheless, sugar was only to be found from seven to twelve hours after death. Two of the instances occurred in mammals, the third in a bird.

It may be added, as the result of my general experience in reference to the point under consideration, that in the liver of a rabbit which may happen to contain a large amount of amyloid substance there is not so rapid and extensive a production of sugar after death as in the liver of a dog containing a much smaller amount of it. It would seem, indeed, that the larger the amount of amyloid substance, the less freely and rapidly does the *post-mortem* saccharine metamorphosis ensue.

If it is exceptional for amyloid substance not to undergo metamorphosis into sugar in the *liver* after death, instances can be given from amongst the lower animals where it exists, not merely as an embryonic and temporary, but as a permanent, constituent in other parts without a similar proneness to change being observable. I have already stated that I have met with amyloid substance in large quantity in the mantle of the mussel. In this situation it does not undergo the same *post-mortem* transformation into sugar that it does in the liver. It may be put down, I think, that it exists here without any ferment in contact with it; for under the influence of exposure to the action of a ferment, as for instance saliva, a copious production of sugar is found to ensue. The amyloid substance seems to form in this locality a store to be drawn upon during the development of the ova; for, whilst the mantle is thick and opaque, and highly charged with it previous to spawning, it is thin, watery looking, and comparatively devoid of it afterwards.

The fact has also been pointed out by Dr. Michael Foster ('Proceedings of the Royal Society,' No. 79, 1865) that amyloid substance exists largely in the bodies of certain entozoa; and that, as in the case of the mantle of the mussel, it is here not prone to undergo transformation into sugar after the death of the animal, except under the addition of a ferment. In the bodies of both the round-worm and the tape-worm, for instance, it has been encountered in considerable abundance, and these animals have been exposed to a warm temperature for many hours after death without any appreciable production of sugar having been found to take place. It is a striking circumstance, as has been remarked by Dr. Foster, that it should thus exist in animals whose natural habitat is in the midst of juices which possess a strong fermentative power, and yet that no transformation into sugar should be found to occur.

Under ordinary circumstances, certainly in the liver, the position of the amyloid substance is such that it rapidly passes, in compliance with chemical laws, into sugar after death—that is, a ferment is then allowed to come into play and effect a change which does not occur during life. The blood, amongst other constituents of the body, is found to act as an energetic ferment upon this principle. Amyloid substance mixed with the blood outside the body is rapidly transformed into sugar. Amyloid substance, also, brought into contact with the blood as it is circulating in the body, becomes similarly transformed into sugar; and hence, by injecting it into the circulation of a living animal, a saccharine condition of the system is brought about, and if enough be employed the urine may be thereby made to acquire a strongly saccharine character.

By causing the blood to be detained in the liver after death a much larger production of sugar takes place than would otherwise occur. Indeed, in order to obtain a strongly marked result, in repeating Bernard's experiment for showing the presence of sugar in the liver, it is requisite not to open the vessels and allow the blood to escape from the organ too early. It must be understood, however, that it is not alone by the agency of the blood that the amyloid substance is converted into sugar in the liver, for, after the whole of the blood has been washed out of the organ by a stream of water passed through its vessels, a gradual production of sugar is still found, as has been previously pointed out, to occur.

It is certainly difficult to understand how the amyloid substance should escape, as it does, transformation into sugar during life, and yet be transformed with such activity so speedily after death; but still there is the fact, and we are bound to accept it, however much astonishment it may excite. We are, however, it may be said, not unprepared for such an event, seeing that a parallel is presented to us in the phenomenon of the coagulation of the blood. Blood, as is well known, exists in a state of fluidity whilst it is contained in the living system, but coagulates, or assumes a solid form, almost instantly after withdrawal. Now, we have here a phenomenon of quite as striking a character as that which has been referred to as occurring in the liver, and, moreover, the effect of the altered circumstances shows itself with a like rapidity in the two cases. As regards the blood, the alteration in its condition that ensues upon withdrawal is too self-apparent to admit of any question about it, and it thus affords unequivocal evidence of the almost instantaneousness of the change—a change, too, of a most decided nature—that may be brought about by the influence of altered circumstances. The fact of coagulation is sufficiently obvious; but as to the cause of it, it must be considered that we are still without a satisfactory explanation. It is true, according to the information that has been recently obtained upon the subject, fibrine has no existence in fluid blood, but is formed at the moment of coagulation, by the combination of a couple of principles that have received the names of fibrinogen and fibrino-plastin, the latter constituting the body which has long been known under the name of globulin.

Both these principles are contained in fluid blood. They do not unite as long as the blood is circulating in the living system, although they do so immediately after its withdrawal. Now, how it happens that these principles combine to form fibrine, as they do, under the one condition, and yet are kept apart under the other, constitutes as difficult a problem for solution as how it happens that amyloid substance escapes transformation into sugar during life, and yet is transformed immediately after death.

According to a recently expressed opinion of Schiff, amyloid substance is not transformed into sugar during life, because the ferment does not exist. The ferment, he affirms, only becomes developed at the moment of death, and thus it is that a production of sugar only then ensues. My own experiments, however, do not enable me to endorse this view.

Amyloid substance, as has been stated, is contained in the hepatic cells; and it has further been mentioned that any escape and admixture with the blood immediately gives rise, according to my own experience, to a saccharine condition of the circulation. How is it, then, it may be asked, the blood circulating in such close proximity as it does to the hepatic cells, that amyloid substance does not pass into it, and give rise to a saccharine condition of the system? The explanation is to be found in the physical property of non-diffusibility which amyloid substance enjoys, and a good illustration is here afforded of the harmony that exists in the adaptations of nature.

Had we in the amyloid substance a principle to deal with holding the position of sugar as regards the property of diffusibility, the blood could not circulate through the liver without carrying it away. In wise harmony, however, with the requirements of the case, this substance belongs to the group of colloids, or non-diffusible bodies. On placing a mixture of sugar and amyloid substance together in a dialyser, the sugar will be found to diffuse, whilst the amyloid substance remains behind. I have found, even under the influence of the pressure of a column of fluid six feet high, that amyloid substance has failed to pass through an ordinary piece of bladder.

Now, albumen is also a material which agrees with amyloid substance in possessing a low degree of diffusibility. Submitted to experiment, it does not pass, to any extent, through a thick membrane, such as a piece of bladder, except under the influence of a considerable amount of pressure. By such a property its retention in the blood-vessels is provided for. There would be a want of harmony in the circumstances of the case if a material intended to serve as a pabulum for the nutrition of the tissues, and, therefore, required to be retained in the system, should have a tendency like, for instance, sugar and urea, to escape from the blood by being endowed with the property of diffusibility. And so with regard to the amyloid substance of the liver, its want of tendency to diffuse may be taken as affording in a converse way presumptive evidence that it is not intended to pass from the hepatic cells into the circulation.

By the property of non-diffusibility which the amyloid substance enjoys the system is prevented from becoming saturated with sugar, as under an opposite condition would occur. Under a natural state of things it is certain that amyloid substance can neither pass into the blood-vessels nor be transformed in the liver into sugar to more than an almost inappreciable extent, on account of the insignificant amount of sugar which the blood is found to contain. Under certain unnatural circumstances, however, amyloid substance is transformed into sugar during life, and this principle, finding its way into the circulation, makes its appearance in the urine. It is to this point—in other words, to the pathology of diabetes—that I purpose now to direct attention.

PATHOLOGY.

Diabetes (διαβαινω *to pass through*), taken in its literal acceptation, signifies an excessive flow of urine from the system. This, it must be admitted, forms one of the most common and prominent features of the complaint under consideration. It does not constitute, however, an invariable accompaniment—does not invariably exist, that is to say, in all forms and stages of the disease. Taken alone, also, it does not serve to characterise the complaint, for cases occur in which a marked and continuous excessive flow of urine is noticed without forming cases of the disease in question. With the increase in quantity, an unnatural state, as regards quality, exists, a principle, viz. sugar, which ought not to be discoverable to any appreciable extent in the urine, being encountered in notable amount as a constituent. At the time the term diabetes was first employed nothing was known about the existence of this unnatural quality of the urine. When it was discovered, the adjective "*mellitus*" was added, to distinguish the class of case in question from that in which an excessive flow of urine (polyuria) is met with without the passage of sugar—a form of disease that falls under the denomination of *diabetes insipidus*.

It has been said that the disease is accompanied with the passage of sugar with the urine. This phenomenon, indeed, constitutes an essential feature of the complaint. A case to be pronounced as one of diabetes mellitus must be attended, in some part of its course, if not throughout, with the discharge of sugar from the system with the urine. The presence of sugar in the urine, however, does not necessarily denote that diabetes mellitus exists. Glycosuria, or the passage of saccharine urine, may be produced by other conditions than the existence of diabetes. There may be, as will be amply shown further on, a temporary appearance of sugar in the urine without diabetes mellitus existing. Thus, glycosuria, which simply signifies passage of sugar with the urine, is not synonymous with diabetes. Every case of diabetes mellitus is necessarily one of glycosuria, but the converse does not hold good—that is, glycosuria may be encountered without the existence of diabetes.

Willis, about the year 1674, was the first to announce that the urine in diabetes possessed a sweet taste. A century, however, elapsed before the saccharine principle was isolated, it being by Cowley, in 1778, that this was first effected. Now, before proceeding further, let us pause to inquire whether sugar, to any extent, forms a constituent of healthy urine. Seeing, as has been mentioned under the head of physiology, that a trace of sugar exists in the circulatory system, and likewise looking at the property of high diffusibility that sugar enjoys, I inferred, without being aware that it had already been shown to be a fact, that a trace of sugar should be discoverable in healthy urine. In one of my Lettsomian lectures delivered at the Medical Society and published in the 'Lancet,' in 1860, I thus expressed myself upon the point:—"I should say even that the trace of sugar, which is natural to the blood throughout the body, is constantly being drawn upon by the kidney; but that the amount for removal is so small that it is not susceptible of detection in the urine. Did we possess more perfect means of detection than we do, I imagine a minute trace of sugar would be reckoned as a normal constituent of the urine. I am speaking now a little problematically, but what I have said accords with the principle that has been forcibly recognised in analytical chemistry, namely, that the minuteness of diffusion of materials through the different constituents of the universe exceeds or surpasses our powers of detection."

Tested ordinarily, no reaction of sugar is certainly to be found, but Brücke, by operating upon a considerable quantity of urine, and treating it so as to get rid in great part of other ingredients, has shown that sugar must be ranked as a constituent to a minute extent of normal urine. Dr. Bence Jones has repeated Brücke's analysis, and confirmed his statement. In the 'Medical Times and Gazette,' January 21st, 1865, he states that he had satisfied himself by the most careful investigation that Professor Brücke is right in saying that healthy urine contains sugar.

It may be mentioned, *en passant*, that this discovery of the existence of a trace of sugar in healthy urine supplies still another argument against the glycogenic theory. If from the trace of sugar naturally existing in the blood, sugar is susceptible of recognition, as has been shown by Brücke and confirmed by Bence Jones, in the urine, what, it may be asked, would be the condition if sugar were poured in quantity into the circulatory system, in accordance with the doctrine of glycogenesis? Sugar, arriving in the general circulation, does not suffer destruction in the lungs, as was formerly supposed, but reaches the arterial system, by which it is conveyed to the kidney as well as the other parts of the body. By virtue of its diffusibility it must then pass off with the urine. Sugar, it may be asserted, cannot exist in the general circulation without being drawn upon and discharged by the kidney; and hence, sugar formation by the liver would constitute a purposeless or fruitless process. Now, apart from other considerations, it can hardly be considered probable that sugar should be formed by the liver to be thus immediately got rid of by the kidney.

The urine in accordance with what has just been stated, takes its character from, and, it may be said, furnishes an index of, the state of the blood; and directly sugar, to any notable extent, finds its way into the vascular system, the urine is sure to become correspondingly saccharine. Hence, from this it follows that if sugar escaped from the liver, as was formerly supposed, the result would be that we should all of us be passing saccharine urine—in other words, that we should all of us be in the position of the diabetic.

It is not uncommon, as a matter of clinical experience, to meet with more than a trace of sugar in the urine without diabetes existing. It has been previously mentioned that the urine of patients is not unfrequently found to give more or less reaction with the cupro-potassic solution without being submitted to concentration, or subjected to any special process for testing. The urine of a large number of patients, labouring under various complaints, was upon one occasion tested by the clinical clerks at Guy's Hospital and found, in several instances, particularly in cases of phthisis, to give a more or less marked reaction of sugar. With some specimens, indeed, quite a fair amount of reduced oxide was thrown down upon being boiled with the cupro-potassic solution.

Looking now to diabetes, the question may be asked, whence comes the sugar encountered in the urine? The kidney was the organ that was formerly thought to be at fault, the view entertained being that, by some peculiar irritation or modification of its functional activity, the sugar was produced by it out of the elements of the blood circulating through its vessels. It was subsequently discovered, however, that the sugar existed pre-formed in the blood, and thence it followed that the only share taken by the kidney in the disease was the discharge of this principle from the system. The kidney, it is certain, must be acquitted of exerting anything beyond a simple eliminative action, and in separating a material like sugar from the blood it is only acting in a perfectly natural manner.

The statement, when first made, that the sugar existed in the blood, was received with doubt. Analytical chemistry was not then in the position that it has since attained. The means that were formerly known of for detecting sugar were far less efficient than those at our command at the present day. Crystals of sugar, it was affirmed, had been obtained, together with a syrupy non-crystallizable liquid which underwent fermentation with yeast. McGregor, of Glasgow, confirmed this statement. By coagulating and drying off the serum of diabetic blood, and then boiling it in water, and concentrating the decoction, he obtained a syrupy fluid which fermented strongly with yeast. Nowadays the tests at our disposal for detecting sugar leave no doubt about its existence in diabetic blood.

I have several times myself examined the blood of diabetics that had been removed by cupping and venesection, and have found it sufficiently charged with sugar to cause it to give a copious orange-yellow reduction with the copper solution. Upon one occasion I made a quantitative analysis of a specimen of blood that had been abstracted from the loins by cupping, and the amount of sugar indicated was 53-100ths or just over half a grain per cent. This is equivalent to about 2½ grains to the fluid ounce. As stated above, the sugar has been procured from the blood in a crystalline state, and I have so obtained it myself.

It being thus ascertained that the sugar is susceptible of recognition in the blood, a step in advance has been made, but the question still presents itself, whence does it take its origin? Towards the close of the eighteenth century Rollo set forth the opinion that diabetes was due to an imperfect digestion—to a derangement having its seat in the stomach, and attributable to a peculiar alteration in the gastric juice, which had acquired the alleged morbid property of changing into sugar the vegetable materials ingested. It was afterwards shown, however, by Tiedemann and Gmelin that during the digestion of amylaceous matter sugar is produced as a natural phenomenon. It was also further ascertained by Magendie and others that the portal blood becomes impregnated with sugar when the digestion of amylaceous matter is being carried on. From this it followed that the formation of sugar in the digestive canal from vegetable materials could be no longer legitimately looked upon as forming the source of the sugar in diabetes, because such an event had been shown to take place naturally.

McGregor's experiments gave a new turn to this matter, and revived the question of the digestive canal forming the seat of error in diabetes. That sugar should be recognisable in the alimentary canal after the ingestion of amylaceous matter is naturally to be looked for, because there are secretions which are specially endowed with the power of effecting the transformation of starch into sugar. McGregor, however, found that sugar was also to be detected in the alimentary canal of the diabetic after the ingestion of animal food, from which no sugar is naturally producible. After administering an emetic and a purgative to a healthy and a diabetic person to clear out the alimentary canal, he fed each exclusively upon roast beef and water for a period of three days. At the end of this time the contents of the stomach of both individuals were procured, from three to four hours after a meal, by means of vomiting induced by the sulphate of zinc. The vomited matters from the healthy man yielded no reaction with the fermentation test, whilst those derived from the diabetic fermented, and fermented, it was said, pretty briskly.

From these results the inference was drawn that the seat of production of the sugar met with in the blood and discharged with the urine in diabetes, was the alimentary canal; and a perverted action of the stomach was looked upon as constituting the cause of the phenomenon.

Prout was also of opinion that the seat of error in diabetes was located in the digestive organs. In his work on 'Stomach and Renal Diseases,' fifth edition, p. 38, he says, "The facts and observations I have to offer on the subject are founded on the opinion already advanced, namely, that diabetes is nothing more nor less than a form of dyspepsia; that this dyspepsia principally consists in a difficulty of assimilating the saccharine alimentary principle, and that like all other forms of dyspepsia, whether it be an inherited or an induced affection, diabetes is liable to be much modified and aggravated by concomitant circumstances." Other passages might also be quoted to show that he regarded diabetes as the result of a defective action of the stomach; but in a note at page 37 he brings the liver into the question, by saying, "Functionally speaking, I am induced by long attention to believe that the liver is always deeply involved in diabetes." From what is stated in the text, however, this remark has to be construed as implying that he believed the liver to be involved by the constant passage of sugar through its vessels, and not that it was primarily implicated in the complaint.

The sugar met with by McGregor in the vomited matters of the diabetic did not necessarily originate in a faulty performance of digestion. The blood of a diabetic being saccharine forms enough to give rise to a saccharine condition of the secretions. All the secretions, it is true, are not thereby rendered saccharine, but from Bernard's results it seems that the gastric juice unquestionably is so. For instance, Bernard states that in the vomited matters of a diabetic at a period of fasting he has been able to recognise the presence of sugar. Gastric juice being secreted in a saccharine state will at once account for the presence of the sugar in the vomited food of McGregor's patient, without the necessity of falling back upon any perverted action of the stomach. The notion, it may be added, about faulty digestion giving rise to the sugar in diabetes receives no support from the researches of modern times, and may be looked upon, indeed, as entirely devoid of foundation.

As regards the presence of sugar in the secretions of the diabetic, the following remarks may be made. It was detected in the alvine evacuations by McGregor, and crystals of sugar even were obtained. Although present in the gastric juice, it is not to be met with, according to Bernard, in the saliva, the pancreatic juice, the tears, the sweat, or the bile. Respecting the sweat, Dr. Parkes observes, in his work on the 'Urine,' at page 353, "That sugar is found occasionally in the sweat is generally admitted. Fletcher ('Medical Times,' 1847, page 394) obtained in forty-eight hours $6\frac{1}{2}$ grains of sugar from a piece of flannel three inches square, placed in the axilla. In one of my patients, a boy without phthisis, who was made to perspire profusely by the hot-air bath, Ranke found no sugar." The cerebro-spinal and serous effusions, Bernard says, are charged with sugar when it exists distributed through the system, as it does in diabetes. Lehman affirms that he has found sugar in the saliva during diabetes, but Bernard suggests that it is necessary not to confound mucus from the lungs, which contains sugar, with true saliva. I have myself examined the saliva in two cases of diabetes; in one of them I found no evidence of the presence of sugar, whilst in the other my test afforded an indication of the existence of a trace.

Upon one occasion I examined some pus derived from a diabetic subject—the case was that of a girl between twelve and thirteen years of age. The pus was obtained from an abscess situated upon the head, and it yielded evidence of containing sugar.

Seeing from what has preceded that there are no grounds to show that the sugar encountered in diabetes is formed in the digestive tract, we are brought back to the position we were in before McGregor's experiments were conducted. The sugar, it has been ascertained, exists in the blood, but whence this sugar comes, again, presents itself as an open question for consideration.

Bernard's experiments next claimed attention, and pointed to the liver as forming the seat of production of sugar in diabetes. According to Bernard's glycogenic theory, the liver was looked upon as enjoying a sugar-secreting function, the sugar produced being supposed to undergo subsequent destruction in the lungs. It was thought that these processes balanced each other, and thus that there resulted no accumulation of sugar in the system. Now, under the view that these processes of sugar-secretion and sugar-destruction were being constantly carried on as natural phenomena of life, diabetes was considered to be due either to an excessive formation of sugar on the one hand, or a defective destruction on the other—either, that is, to the production being in excess of the capacity for destruction, or the production remaining within ordinary bounds, to a diminished power of destruction. In accordance, however, with what has been shown in a former part of this work, these processes have not the reality that was formerly supposed, the conclusions upon which the presumption of their existence was founded proving to be fallacious.

The question of sugar-secretion by the liver, and sugar-destruction in the lungs, as processes of physiological occurrence, must thus be discarded from consideration in reference to the pathology of diabetes. There ought to be no sugar of any account entering the circulation; should there be any it may be put down as originating in some unnatural condition, and its presence will immediately occasion, according to its extent, a more or less highly saccharine state of the urine. Indeed, the saccharine element derived from our food ought to be assimilated, and prevented from reaching the general circulation. No matter, it may be said, from what source the sugar is derived, the result of experimental inquiry justifies the assertion that whenever it reaches the general circulation it is sure to pass off with the urine. There is no part of the circulatory system in which sugar is known to undergo any appreciable amount of destruction. Sugar that has once escaped from the liver is to be detected alike in the blood throughout all parts of the circulation.

Under the supposition that sugar was produced in the liver and destroyed by oxidation in the lungs, defective oxygenation was looked upon as constituting a cause of glycosuria. Bernard himself says that he had thought at first, in conjunction with others, that the diabetic state following his experiment of puncturing the *medulla oblongata* was produced by an implication of the respiratory centre, leading to an imperfect combustion of the sugar supposed to be passing through the lungs. From subsequent research, however, Bernard admitted that this view stood at variance with the facts of the case. Reynoso and Dechambre were to be found amongst the supporters of the defective oxidation theory. They asserted that a certain quantity of sugar was to be encountered in the urine of the aged, and referred its presence to the diminished activity of the respiratory process belonging to this period of life. There is not, however, as far as I am aware, any evidence producible to show that sugar is susceptible of undergoing direct oxidation in the system, or that, as sugar, it is capable of contributing towards heat-production.

The idea was started by Liebig, before Bernard's experiments were conducted, that sugar underwent a process of combustion in the lungs, and thus contributed towards the maintenance of animal heat; and the idea harmonised with the doctrine of glycogenesis, because a useful purpose was provided for the sugar supposed to be produced by the liver. It must be stated, however, that Liebig's idea has no foundation in fact, and Dr. Prout at an early period (as is shown by the following passage found as a note at page 459 in the fifth edition of his work on 'Stomach and Renal Diseases') expressed himself in very strong terms against it:—"The reader will observe that in the above, as well as in other parts of this volume, I have advanced an opinion regarding saccharine aliments totally at variance with the prevailing doctrine of the day, viz. that the only use of the saccharine class of aliments is to form animal heat by combustion in the lungs. I regard this hypothesis in its literal and general sense as utterly at variance with the experience and common-sense of mankind, and have no doubt that future physiologists will look back with wonder that anything so absurd should have been advanced, much less adopted, in the present 'enlightened' age."

Not only did Liebig's theory of sugar combustion harmoniously fall in with the doctrine of glycogenesis; but, conversely, a portion of the experimental evidence adduced in connexion with glycogenesis stood in support of the sugar-combustion theory of Liebig. The experimental evidence to which I allude is that which seemed to indicate that a destruction of sugar really took place in the lungs. It has been shown, however, how this evidence has turned out, under further inquiry, to be based upon a fallacious foundation, inferences having been drawn from experimental results which they do not, strictly speaking, justify. Acting upon the present knowledge we possess of the sources of error to be avoided, it is no longer found that the difference formerly believed to exist in the blood on the opposite sides of the lungs is in reality to be discovered. Whatever sugar is present in the blood of the right side of the heart will, as far as can be ascertained by close examination, be present also after the blood has traversed the lungs and reached the arterial system. Hence, without any provision for the disposal of sugar, if the liver possessed a glycogenic function, the sugar presumed to be produced would necessarily accumulate in the blood; and, thence, by virtue of its diffusibility, would make its appearance in the urine, as in reality is the case in diabetes in contradistinction to what is noticed under a normal state of things.

Without accepting Bernard's glycogenic theory, an abundant array of evidence can be brought forward pointing to the liver as forming the seat of error in diabetes—pointing, in other words, to a faulty action of the organ as giving rise to the sugar encountered in the complaint.

Glycosuria, in the first place, is susceptible of being produced by direct injury of the liver. Bernard, in his 'Leçons de Physiologie Expérimentale,' (Paris, 1855, p. 346) relates a case in which a saccharine state of the urine was observed to follow a blow over the region of the liver. He says—"On me citait dernièrement le cas d'un individu qui avait reçu un coup de pied de cheval dans l'hypochondre droit, et qui, à la suite de cette blessure, avait présenté du sucre dans ses urines; mais ce symptôme avait disparu lorsque le malade avait été guéri de sa contusion, seulement il était resté polyurique."

Fischer also ('Archives Générales de Médecine,' tome xx, 1862, p. 441) quotes a case in which a nightman received a blow from the shafts of a vehicle in the right hypochondriac region. He was taken to the Hôtel-Dieu, and placed under the care of M. Laugier. Soon afterwards there was vomiting of blood, which, upon ceasing, gave place to temporary diabetes. The diabetes existed during the first fortnight after the accident, the presence of sugar in the urine being attested by Bouchardat. The sugar disappeared with the disappearance of the signs of contusion of the liver, but the patient was afterwards transferred to M. Rostan's care suffering from polyuria, or diabetes insipidus. Of this he got better, but in the course of a year the complaint returned, and the urine was found to contain traces of sugar. Some time afterwards the urine is reported as being again devoid of sugar, and ultimately also it became reduced in quantity to the normal point.

Schiff states that he has obtained temporary diabetes by passing needles into the liver; and I have myself produced the same phenomenon by the action of galvanism upon the organ. My object in thus experimenting with galvanism was to try the effect of applying the poles of the battery so as to get a liberation of acid in the liver and alkali in the stomach, thus reversing the natural order of events occurring as the result of secretion. A five-celled Grove's battery was employed in the experiments, the positive pole being inserted into the liver, and the negative pole introduced into the stomach. The urine in from one to two hours' time was found to have become strongly charged with sugar. I afterwards noticed, contrary to what I had anticipated at the outset, that reversing the position of the poles was followed by the same result; and likewise, even, that glycosuria was produced by operating solely on the liver, *i. e.* after both poles had been inserted into the substance of the organ. It may, therefore, be considered that the saccharine urine noticed in these experiments arose, as in Schiff's experiment with the needles, from the effect of direct irritation of the liver.

In the next place, the artificial diabetes observed to follow the removal of the superior cervical ganglion of the sympathetic fails to be recognisable after the application of a ligature to the portal vein and hepatic artery, so as to stop the flow of blood through the liver. Now, assuming the sugar to be derived from this organ, such a result is just what might be looked for; as, from the nature of the operation performed, the saccharine principle must necessarily be prevented from escaping to reach the circulation and make its appearance in the urine.

In harmony with this observation of my own is one that has been made by Schiff upon frogs, which, Bernard remarks, may be taken as almost incontestably showing that the sugar encountered in diabetes is derived from the liver. Schiff discovered that Bernard's puncture of the *medulla oblongata* was followed by the production of glycosuria in the frog as well as in the higher animals. Schiff took twelve frogs and submitted them to the operation of puncturing the *medulla oblongata.* Six of them were left without anything further being done, and in these he observed the urine became charged with sugar. In the other six the vessels of the liver were ligatured, and no sugar was to be discovered in the urine. The ligatures were then removed, and in the course of a few hours the urine was found to have acquired a saccharine behaviour.

Further support is given to the proposition which places the liver in the position that has been mentioned, by the disappearance of sugar that is frequently observed to take place from the urine of diabetics shortly before death, and under the supervention of acute disease. It has been already pointed out in a previous part of this work that the amyloid substance which is found to be contained in the liver under normal circumstance, disappears from the organ under morbid conditions of the system. Now, looking upon this amyloid substance as constituting the source, by undergoing a downward or retrograde matamorphosis, of the sugar in diabetes, the disappearance of the sugar from the urine of diabetes under the circumstances mentioned accords with what might be looked for. I could cite numerous examples that have fallen under my observation, where the disappearance of sugar referred to has been noticed to take place. I have seen cases in which persons labouring under diabetes have been attacked with smallpox and typhus fever, and have witnessed a disappearance of sugar from their urine. I have also several times noticed that the urine of diabetics, where death has taken place from the disease, has become devoid of sugar a short time previous to dissolution.

It must not be inferred, however, from what has just been said, that there is anything more than a frequent disappearance of sugar from the urine under the circumstances named. I have before me a record of several cases in which sugar was recognisable in the urine up to the time of death, and in the solids and fluids afterwards. I have also the notes of a case in which sugar continued to be discharged throughout an attack of typhoid fever. The patient in question became affected with fever during the occurrence of an outbreak in one of the wards of Guy's Hospital, and was confined to his bed for several days, but ultimately recovered. His urine was submitted to frequent examination, and always found to contain sugar.

In reference to the supervention of fever upon diabetes, I may remark that, according to what I have seen, a diabetic is more liable than others to be affected by exposure to infection, and, at the same time, less likely than others to recover when affected. Should the sugar disappear during the supervention of an acute disease, and recovery afterwards take place, a reappearance may be confidently looked for as the acute disease subsides.

Dr. Wilks, who has had a large experience in the post-mortem room, is of opinion that the diabetic liver presents certain physical characters by which it may be recognised. It is, he says, dark in colour, firm and tough in consistence, and homogeneous or uniform in appearance. Nothing special, however, is displayed by the microscope. I do not know whether it has any significance, but I have noticed, in several instances, that the bile has presented an abnormal appearance, having been found quite thick or turbid in character, and of a red or brownish-red colour. On standing, also, it has allowed a pretty copious sediment to subside, which, examined microscopically, has been found to consist of yellow amorphous or granular-looking matter with columnar-shaped epithelial cells.

I think, then, it may be considered that the liver forms the organ to which we must look in diabetes for the source of the sugar that appears in the blood, and thence is discharged with the urine. Now, there are various known conditions that will give rise to glycosuria, and these it will be desirable to speak of before referring to diabetes as it is found to occur in the human subject.

As has been shown under the head of Physiology, it is the office of the liver to detain and convert into another principle the sugar derived from the food and absorbed from the alimentary canal. Sugar forms one of the natural elements of our food. It is absorbed from the digestive canal by the portal vessels, and carried to the liver. Should it pass through and arrive in the general circulation, it will be sure to be discharged from the system with the urine. Under natural circumstances, however, such a result does not take place. The sugar is stopped by the liver and assimilated or transformed in such a manner as to be rendered applicable in the economy to the purposes of life.

Now, observation shows that even in the healthy individual the power of assimilating sugar is not unlimited. The sugar ingested, it is true, under ordinary circumstances, does not appear in the urine; but if an excessive quantity be consumed, and especially at a period of fasting, when absorption is more rapidly carried on than at other times, a portion escapes being detained by the liver, and, reaching the general circulation, makes its appearance in the urine. It will be remembered that in the dogs, referred to in a former part of this work, that were fed upon animal food and sugar, the urine in three out of the four presented a saccharine behaviour. In the experiments on the rabbits, also, referred to at p. 98, the urine after a few days' feeding on an exclusive diet of starch and sugar was found to contain sugar.

What has just been stated accords with the results that have been obtained by Bernard, who remarks that the urine of an animal may be rendered temporarily saccharine by causing a large quantity of sugar to be ingested at a period of fasting. He says that glycosuria may be induced in a rabbit by allowing it, after fasting for a day, to eat freely of carrots. He has also similarly noticed the occurrence of glycosuria in the human subject, a temporarily saccharine condition of the urine having been induced by the ingestion of a large quantity of syrup the first thing in the morning upon an empty stomach.

It is worthy of remark that in these cases, no matter whether cane-sugar or grape-sugar has been ingested, it is grape-sugar that appears in the urine. If cane-sugar should happen to reach the general circulation, either as the result of direct injection into a blood-vessel, or by absorption from the subcutaneous tissue into which it may have been introduced, it will appear as cane-sugar in the urine; but absorbed from the alimentary canal, and thus made to traverse the liver, it will be transformed and appear as grape-sugar, should it appear at all, in the urine.

Sugar, it will be observed, in this respect, stands in the same position as albumen. Both form alimentary principles that ought to be detained in the system. As with sugar, albumen ingested in an excessive quantity at a period of fasting may show itself in the urine. An instance is recorded by Bernard in which the ingestion of six eggs in a raw state after several hours' abstinence was followed by an appearance of albumen for a short time in the urine. As with sugar, again, albumen introduced directly into the general circulation passes off with the urine; whilst, received in a natural manner into the alimentary canal, it is retained and applied to the purposes of the economy.

An illustration has thus been supplied of one way in which glycosuria, or saccharine urine may be induced. Consumed in the ordinary manner, and within ordinary limits, sugar is assimilated and applied to the purposes of the economy. The power of assimilating sugar, however, is not unlimited, and hence it arises, even in the healthy subject, that when an excessive quantity is ingested a portion escapes undergoing the proper conversion, passes through the system, and makes its appearance in the urine. It may be considered that under these circumstances the sugar is absorbed with such rapidity as to be conveyed to the liver in too large a quantity to be completely arrested by the organ and thereby prevented from reaching the general circulation.

In harmony with this we have the effect of introducing sugar directly into a branch of the portal system. I have noticed, for instance, as the result of its injection into one of the mesenteric veins, that the urine has speedily presented a saccharine behaviour. Thus it happens that sugar conveyed in limited quantity by the portal blood to the liver, as it is, for instance, after absorption from the alimentary canal under ordinary circumstances, is completely stopped by the organ, and prepared by it for utilization in the system. Reaching the liver, however, in larger quantity; whether as a result of rapid absorption, in consequence of its copious ingestion during fasting; or whether as a result of direct introduction into a branch of the portal vein, a portion passes through with the blood, and, arriving in the general circulation, makes its appearance in the urine.

Now, cases of diabetes are met with in which all the error that exists seems to be a want of the proper amount of assimilative power over sugar. In some of these cases there is a total loss of assimilative power, so that should any starch or sugar be ingested sugar will appear in the urine. In others there are various degrees of diminution. A certain quantity of starch or sugar may be consumed without the urine being rendered saccharine; but should this quantity be exceeded, glycosuria will be immediately observed to result. Such cases as these are not uncommon among elderly people; and as long as, by attention to diet, the urine is kept free, or nearly free, from sugar, no deviation from an ordinary state of health is to be perceived.

In the majority of cases, however—in the bulk of the cases, it may be said, occurring amongst the young, and below the middle period of life—there must exist something besides a want of power to assimilate sugar, for the diet may be such as to secure a total exclusion of starch and sugar from the food, and still the urine shall be charged, and, it may be, to a considerable extent, with sugar. To account for this we must look to the amyloid substance of the liver, which, with the data before us, may be reasonably regarded as forming the source of the sugar that appears in the urine. It has been shown under the head of Physiology that in the amyloid substance, we have a principle which exists largely in the liver, and which, as one of its chemical properties, is exceedingly prone to undergo metamorphosis into sugar. Normally, this metamorphosis is prevented from taking place to more than a barely appreciable extent; but under various unnatural circumstances it is more or less freely allowed to occur, and, as the result, sugar appears to a corresponding extent in the general circulation, and from thence finds its way into the urine.

The unnatural conditions thus leading to the transformation of amyloid substance into sugar will now form the subject of consideration. They may be conveniently grouped under the following heads :—

1. The state of the blood-vessels.
2. The blood.
3. Lesions of the nervous system.

First, then, as regards the blood-vessels. Under normal states of the circulation the blood passes through the liver without, certainly to any significant extent, disturbing the amyloid substance contained in the hepatic cells. Amyloid substance, as has been mentioned, forms a principle which offers resistance to traversing animal membranes, and hence its capacity for retention in the liver, notwithstanding its close proximity to the circulating current. Still, that it *can* pass from the liver-cells into the blood-vessels is proved by the effect, already referred to, of injecting a stream of water through the vessels of the liver after death. The water which has thus traversed the organ is found to be more or less charged with amyloid substance. Now, suppose such an escape of amyloid substance to occur during life, sugar, to a corresponding extent, will be immediately susceptible of recognition in the blood, and will appear accordingly in the urine.

We have here, it seems, an illustration of the manner in which saccharine urine is, in reality, sometimes occasioned. For instance, sugar is found, as a matter of experience, to make its appearance in the system under violent muscular efforts, and, likewise, under congestion of the vessels occurring as the result of obstruction of the breathing.

Bernard, it may be stated, remarks that whilst the blood withdrawn from the jugular vein of an animal in a state of tranquillity contains only a trace of sugar, that which is removed from the same animal after compression of the abdomen, so as to exert pressure on the liver, or after violent contraction of the abdominal muscles and diaphragm, provoked by holding the nose for a few instants, so as to stop the respiration, will be found to be charged with sugar.

I have also noticed in some experiments, specially performed with reference to this point, that Bernard's remark has been confirmed. After obstructing the breathing of a dog for half an hour to an extent short of producing death by asphyxia, the blood was found to present a strongly saccharine behaviour, whilst, previous to the experiment, it only contained the ordinary trace of sugar. In one case the obstruction of the breathing was continued for an hour, and a strongly saccharine state of the urine was observed to be thereby produced. The urine was collected and tested before the experiment was commenced, and ascertained to be perfectly devoid of sugar. At the end of it, it gave a copious orange-yellow precipitate with the copper solution.

In explanation of this effect it may be said that by violent muscular efforts the liver will be compressed, and the escape of amyloid substance from its cells promoted. During the existence of congestion an unnatural relation between the contents of the cells and the blood-vessels will subsist, and changes may thus take place that would not otherwise occur. Besides, also, the effect of detention of the blood in the vessels will be to compress the liver-cells, and favour a transudation of their contents.

Instances can be adduced where glycosuria in the human subject may be looked upon as resulting from these physical causes. For example, in whooping-cough, pneumonia, and coma, a saccharine condition of the urine has been sometimes observed.

In whooping-cough the protracted paroxysms of coughing not only occasion a great amount of venous congestion, as is indicated by the state of the countenance of the patient, but the liver at the same time must suffer compression from the violent action of the abdominal muscles.

In pneumonia, where a large mass of lung tissue is suddenly involved, great dyspnœa will form a concomitant. As a secondary consequence there will be a proportionate obstruction to the passage of blood through the lungs, and a corresponding amount of general venous congestion will thence ensue. The liver will necessarily be implicated in common with other parts; and, as the result, in accordance with what has been explained, favorable circumstances will prevail for the production of sugar whilst amyloid substance continues present in the organ, which is only during the early stage of the disease.

In coma, as a consequence of the loss of nervous power that occurs, the breathing becomes laboured and slow. An impediment to the flow of blood through the lungs is thus produced, and, the liver participating in the general venous congestion that ensues, will be placed in the condition that has been referred to. As an example of glycosuria occurring in this way, the following case may be cited. A man, who had been for many years employed as a carpenter at Guy's Hospital, suddenly fell down in the street in an apoplectic fit. He was brought to the hospital in a comatose state. His breathing was stertorous and slow, and there was great lividity of the face. About eighteen hours after he had been seized with the fit some urine was procured for chemical examination. It was found to be not only highly albuminous, but, after the albumen had been separated by boiling and filtration, gave a copious reaction with the copper solution. There was nothing to lead to the supposition that the sugar existed in the urine previous to the occurrence of the attack.

Division of the pneumogastric nerves occasions a great reduction in the frequency of the breathing, and so may give rise to the production of a saccharine state of the blood, and even of the urine. I have before me the notes of an experiment in which such results were observed. The respiration was lowered to an extreme extent, and intense dyspnœa prevailed. Some blood was procured two and a half hours after the performance of the operation, and found to give a pretty strongly saccharine reaction. The urine, also, collected at the same time, was strongly impregnated with sugar. It is not by any direct effect upon the liver that division of the pneumogastrics leads to this result, for, unless marked dyspnœa and congestion ensue, no appearance of sugar in the urine is to be observed.

It has long been known that after the inhalation of ether and chloroform a certain amount of sugar is to be met with in the urine. Reynoso, by whom this fact was first pointed out, referred it to the diminished activity of the respiration, leading to a deficient oxidation of the sugar supposed to exist in the blood flowing through the lungs. It must be mentioned that chloroform itself produces some amount of reducing effect upon the copper solution, and, getting into the blood, may be looked upon as likely to reach the urine; but taking this circumstance into account, it is still considered that sugar appears in the urine, although a different explanation from that which has been mentioned must be given. It has appeared to me that the effect is attributable, and proportioned in intensity, to the struggling and congestion that ensue. It is not upon the length of time that the inhalation is continued that the extent of reaction is dependent. In an experiment I could cite, where chloroform was administered, and its effects maintained for between three and four hours, only a slight amount of sugar was discoverable in the urine. In another experiment, where chloroform had been administered for only twelve minutes, and nothing else had been done, the urine was found to give a strongly saccharine reaction, an orange-yellow precipitate with the copper solution being thrown down. I was certainly astonished at the behaviour thus presented, but there could be no doubt about its having been due to the administration of the chloroform, for some urine had been previously obtained and tested, and was found to give no sign of reaction.

After noticing the above result I was led to look to the state of the urine after the administration of chloroform for surgical purposes in the human subject. The urine in twenty cases taken indiscriminately from the operating theatre of Guy's Hospital was carefully examined by my former pupil, Mr. Lamb. In the following table the results that were obtained are shown. The urine examined constituted the last that was passed before, and the first that was passed after, the inhalation of the chloroform.

Tabular representation of the behaviour of the urine in twenty cases on being tested for sugar with the copper solution before and after the inhalation of chloroform.

No.	Name.	Age.	Nature of operation for which chloroform was administered.	Urine tested with the copper solution.	
				Before chloroform.	After chloroform.
1	Fred. B—	45	Removal of tumour on leg	No reaction	Slight reaction
2	Thos. W—	35	Amputation of penis	No reaction	Moderate reaction
3	Hannah W—	44	Removal of tumour of breast	No reaction	Moderate reaction
4	Richard P—	6	Removal of diseased bone	Slight reaction	Considerable reaction
5	Eliz. C—	38	Removal of tumour on back	Very slight reaction	Considerable reaction
6	Emma T—	12	Amputation of thigh	No reaction	Considerable reaction
7	Louisa B—	25	Amputation of thigh	No reaction	Considerable reaction
8	Jane M—	28	Amputation of fore-arm	No reaction	Considerable reaction
9	George J—	27	Removal of necrosed bone	No reaction	Strong reaction
10	John H—	33	Amputation of foot	Slight reaction	Slight reaction
11	Ann W—	33	Amputation of thigh	No reaction	Considerable reaction
12	Ellen E—	8	Amputation of foot	No reaction	Slight reaction
13	Emma H—	14	Operation for club foot	No reaction	Considerable reaction
14	George W—	$2\frac{3}{4}$	Removal of necrosed bone	No reaction	Considerable reaction
15	Joseph S—	66	Amputation of thigh	No reaction	Strongish reaction
16	Jane W—	36	Removal of necrosed bone	No reaction	Trace of reaction
17	Louisa K—	24	Removal of tumour of breast	Slight reaction	Moderate reaction
18	Eliz. E—	31	Examination of the bladder for stone	No reaction	Considerable reaction
19	Fred B—	45	Amputation of thigh	No reaction	Considerable reaction
20	Charles T—	41	Amputation of foot	No reaction	Considerable reaction

On casting the eye through the foregoing table, it will be seen that, out of the twenty cases, in only one (No. 10) was there no effect produced upon the urine. In most, the reaction given after the inhalation of chloroform was a considerable one; in some, quite a strong one. In four of the cases, it was found that the urine collected *before* the administration of chloroform gave a slight indication of the presence of sugar. Now, as has been previously mentioned, it is not an uncommon occurrence for the urine of patients to behave in this way, and give more or less show of reaction with the cupro-potassic solution without being submitted to concentration or subjected to any special process of preparation. In corroboration of this assertion I may state that the urine of a large number of patients labouring under various complaints was upon one occasion tested by the clinical clerks at Guy's Hospital, and found in several instances—particularly in cases of phthisis—to give a more or less marked reaction. In some of the specimens tested quite a fair amount of reduced oxide was thrown down.

The glycosuria that has been referred to constitutes a result of passive congestion, or congestion produced in a physical way. Something will have to be said further on about hyperæmia, or active congestion arising from an alteration in the state of the vessels themselves through lesions of certain portions of the nervous system, in connection with the causation of glycosuria.

Glycosuria may, in the second place, be produced by an alteration in the quality of the blood. It can be shown by experiment that certain alterations in the state of the blood circulating through the liver may give rise to such a transformation of amyloid substance into sugar as to occasion a strongly saccharine state of the blood, and thence of the urine.

First, it may be said that a supply of portal blood is necessary for amyloid substance to be maintained without undergoing transformation into sugar. As the result of applying a ligature to the portal vein, so as to cause the liver to be permeated only by a current of arterial blood, I have observed that both the liver and the contents of the circulatory system have become strongly saccharine. The liver was treated so as to obtain evidence of the condition existing during life, and the blood was collected from the living animal. The urine in these experiments, I must remark, did not present a saccharine behaviour ; but this is scarcely to be wondered at, seeing that the application of a ligature to the portal vein is followed by such a diversion of blood from the general circulation, owing to the accumulation that takes place in the portal system, that little or no chance is left for any secreting action to be carried on by the kidney.

If we pause for a moment, and look at this result in connection with the glycogenic theory, it will be seen that another argument is afforded standing in opposition to its validity. If sugar were produced and discharged from the liver as one of its functional operations, as was maintained under the doctrine of glycogenesis, it is hardly reconcilable that upon arresting the principal stream of blood through the organ the contents of the circulatory system should be found in so much more highly saccharine a state than under ordinary circumstances. What it appears we are justified in saying in explanation of the effect produced by this operation is, that with a supply of arterial blood only, the changes in the liver fail to proceed in their natural manner, and that the amyloid substance in consequence undergoes a downward metamorphosis into sugar, like what occurs after death, and also under certain other unnatural states during life.

After ligature of the hepatic artery as well as the portal vein the contents of the circulatory system, as might be expected, are not found to become saccharine as is the case after ligature of the portal vein only. All flow of blood through the liver being arrested, no opportunity is afforded for the escape of sugar from the organ. The liver itself, however, I have found to be strongly impregnated with sugar. The requisite process of examination was, of course, adopted to obtain a representation of the condition existing during life.

After ligature of the hepatic artery I have noticed no deviation from the ordinary state. It is an operation that may be performed without giving rise to any serious consequences, and both urine and blood have been found to remain unchanged in character.

It was some time back noticed by Dr. Harley that the injection of small quantities of ether and ammonia into the portal system was followed by a distinctly recognisable appearance of sugar in the urine. M. Leconte, also, has pointed out that a saccharine state of the urine may be induced by the administration of small doses of the nitrate of uranium. I take it, in these cases, that, through the altered state of the blood passing through the liver, an unnatural metamorphosis of amyloid substance into sugar ensues, and so gives rise to the result.

Again, from my own experiments it appears that the introduction of phosphoric acid into the circulation produces such a condition of the blood as to promote the transformation of amyloid substance into sugar to a sufficient extent to give rise to strongly marked glycosuria. In a paper entitled "The influence of an acid in producing a diabetic state of the urine," published in the 'Guy's Hospital Reports' for 1861, I have given the details of a number of experiments which show that a saccharine condition of the urine is producible, not only by the introduction of the agent directly into the circulatory system, as by injection into a vein, but likewise by its introduction into the alimentary canal. The phosphoric acid of the Pharmacopœia constituted the acid that was employed, and an hour's time was found to suffice for the urine to become so strongly charged with sugar as to throw down a copious orange-red precipitate upon being boiled with the copper solution—in other words, to present the behaviour of ordinary diabetic urine.

Schiff ('Journal de l'Anatomie et de la Physiologie,' Paris, 1866) has advanced the opinion that it is to the development of a ferment in the blood that the production of glycosuria may be ascribed. He in the first place asserts that the blood of the living animal under normal circumstances is devoid of ferment capable of acting upon the amyloid substance of the liver; and hence, he says, the escape of this principle from undergoing transformation during life. Instantly after death he believes a ferment to be developed, and to this he attributes the production of sugar that is then observed to take place in the liver; so that, according to Schiff, the non-production of sugar in the liver during life, and its production after death, are to be accounted for by the absence or presence of a ferment in the blood, the development of this ferment taking place immediately after the destruction of life. He goes further, and says that the ferment may also be developed during life by simply keeping the blood in a stagnant condition, and even by retarding its flow in the vessels. To the liver he assigns a passive part in connection with glycosuria. He looks upon the organ as forming the seat whence the sugar proceeds, but affirms that the production of sugar is dependent upon whether or not a ferment happens to be present in the blood.

In reference to this matter it may be remarked that the circumstance has long been pointed out that sugar is to be met with in the urine as a frequent if not an invariable accompaniment of boils and carbuncles. In the first edition of this work I quoted, in illustration of this association, the particulars of a case that I had a short time previously seen recorded in the pages of the 'Medical Times and Gazette.' The patient, a person seventy-three years of age, of a strong constitution, and previously in excellent health, became the subject of hemiplegia during the month of March, and towards the end of the July following, when the paralysis had been for some time diminishing, a carbuncle developed itself in the lumbar region. This became of considerable size, and was long in sloughing out after incision. During the occurrence of sphacelation of the cellular tissue a considerable quantity of sugar was to be found in the urine, and continued to be present as long as the process proceeded, but disappeared as soon as it was over. The hemiplegia still persisted, but the patient otherwise completely recovered his health. It may further be remarked that in association with gangrene, also, where it may be considered that we have an analogous state to deal with, sugar has been noticed in the urine.

Now, Schiff refers to gangrene, and considers the production of the sugar to be due to the development of a ferment in the circulation, as a consequence of the retardation or stagnation of blood that occurs in the implicated part. Upon this point he says a diabetic gangrene is spoken of, and we have no right to deny its existence; but we know also that there exists a gangrenous diabetes, that is to say, a diabetes accompanying the occurrence of gangrene, and arising from a local retardation or cessation of the circulation. He mentions some experiments upon cats, in which he tied all the veins of the anterior extremity that could be seen. Gangrene slowly supervened in consequence of the almost complete stagnation of blood that was induced. By the small quantity of blood that was suffered to enter the general circulation through the inosculating veins from the affected part, a sufficient amount of ferment, he says, was allowed to reach the liver to produce in three or four hours' time a well-marked diabetic condition, which lasted, and even increased, during the following days, whilst gangrene showed itself in a decided form.

I should be glad if my own experimental experience enabled me to endorse the statements of Schiff, as some points that now appear to me obscure upon the subject of glycogenesis would be thereby cleared up. I must reiterate, however, that, according to my own results, amyloid substance brought into contact with blood is transformed into sugar, no matter whether the admixture be effected whilst the blood is normally circulating in the living system or after it has been removed from the body. The blood under both conditions, as far as I can learn, equally acts the part of a ferment. To be certain of the truth of what I am stating, I have recently repeated the experiment of injecting amyloid substance into the circulatory system, care being taken that a state of tranquillity and otherwise normal circumstances prevailed. The result obtained was in strict accordance with what I had obtained before—sugar, in the course of a short time, being susceptible of recognition in the urine.

It must be remarked that it is with amyloid substance as it is with sugar: unless a certain amount should find its way into the circulation the urine will fail to be found perceptibly saccharine, and this for a reason that seems to me sufficiently obvious. According to Bernard, the injection of half a gramme of sugar into the jugular vein of a rabbit is not followed by an appreciable appearance of sugar in the urine. About one gramme (fifteen and a half grains—say) he speaks of as the limit of the amount that can be destroyed in the system of a good-sized rabbit—in other words, as I would myself put it, that can be introduced into the circulation without being discoverable in the urine. The destruction of sugar is here brought forward as an element of consideration in the matter; but it does not follow, as implied by Bernard, that the reason the urine does not present a saccharine behaviour when sugar below the limit mentioned is introduced into the circulation is because it undergoes destruction; for it must be remembered that sugar, whether directly introduced as such, or derived from amyloid substance that has reached the circulation, will be distributed to all parts of the system, and, on account of its diffusibility, will tend to escape from the blood-vessels and impregnate all the solids and fluids belonging to the different parts of the body. Hence it will only be a portion that will appear in the urine; and our tests for sugar, although delicate, necessarily present a limit to their capacity for reacting. The system must needs be saturated to a certain extent with sugar before a sufficient amount can reach the urine to be susceptible of recognition under the ordinary process of testing.

As to the development of a ferment in the circulation under stagnation of the blood, and a retardation of its flow, the experiments that I have performed have failed to give results coinciding with those described by Schiff. I have repeated Schiff's operation of applying digital compression to the abdominal aorta of a rabbit, and have not been able to perceive that there has been any appearance of sugar in the urine. To secure that the circulation was unmistakably arrested, upon one occasion I applied a ligature to both the abdominal aorta and vena cava of a dog, just below the renal vessels. The ligature was allowed to remain for half an hour and then removed. The urine afterwards continued free from sugar, or at the most gave a barely appreciable indication of its presence. A verification was afforded, by means of a *post-mortem* examination, that both the vessels had been effectually ligatured.

Whilst giving attention to this subject the following mode of experimenting suggested itself to me for putting the point in question to the test. It occurred to me that if a ferment, capable of leading to the production of sugar in the manner alleged, were developed in the blood, from its being allowed to become stagnant, the operation of withdrawing blood and afterwards re-injecting it into the circulation ought to occasion the production of a saccharine condition of the urine. I accordingly withdrew ten ounces of blood from the carotid artery of a dog, defibrinated it by stirring, and in a quarter of an hour's time returned it into the circulation. The urine remained devoid of sugar.

As a kind of converse experiment, I have also tried the effect of introducing a ferment by injection into the circulation. Saliva, which is well known to enjoy the power of energetically transforming amyloid substance into sugar, formed the agent employed. One ounce of human saliva was injected into the jugular vein of a rabbit. The urine three quarters of an hour afterwards contained no sugar, and half an hour later only just an appreciable trace. Death resulted in the course of a few hours, and the lungs were found much congested, and pervaded with spots of ecchymosis. From this it is questionable whether the trace of sugar mentioned above did not arise from congestion rather than the direct action of the saliva as a ferment. It is worthy of note that principles endowed with the property of acting as ferments belong to the group of colloids, and hence, not being prone to diffuse, may exist in the blood without reaching the amyloid substance contained in the hepatic cells.

A certain influence from the nervous system may be looked upon as necessary for holding in check, as it is observed to be held, under natural circumstances, during life, the chemical tendency of amyloid substance to undergo transformation into sugar. Under the loss of this influence, which occurs with death, the tendency is allowed to come into unopposed play, and thus a free production of sugar then ensues. When, therefore, the life of an animal is destroyed, the amyloid substance of the liver, on account of the altered circumstances under which it is placed, immediately begins to undergo conversion into sugar, in compliance with the chemical tendency it possesses. The sugar thus produced accumulates in the liver; and if death be occasioned in such a way that the function of circulation forms the last to continue in operation (as is the case under death occasioned by pithing), a portion is carried away from the organ and distributed through the system. Now, if means should be taken to keep up the circulation after death, as by performing artificial respiration, the sugar produced in the liver passes into the blood, is conveyed to the kidneys, and thence makes its appearance in the urine, for urine still continues under these circumstances to be secreted. An hour's performance of artificial respiration, I have found, has sufficed for causing in this way the urine to assume a strongly saccharine character.

After the destruction of life by the woorali poison and strychnine I have noticed, upon keeping up the circulation by the performance of artificial respiration, that the urine has presented a strongly saccharine behaviour. Bernard mentions having observed the same phenomenon in the case of the woorali poison; but Schiff, whilst admitting that glycosuria is producible by poisoning by strychnine, asserts that, when care is taken to secure that the artificial respiration should as closely as possible conform to the natural process, no appearance of sugar is to be observed as long as the heart is kept acting in a perfectly normal way.

There are certain lesions of the nervous systems without the destruction of life, that are followed by the unnatural metamorphosis of amyloid substance into sugar, and the production of saccharine urine. Some years back the startling discovery was made by Bernard that an artificial diabetes could be induced by puncturing a particular part of the medulla oblongata, namely, a spot comprised in the median plane of the fourth ventricle, just above the line of escape of the pneumogastric nerves.

It may be of interest to mention the way in which this curious fact was brought to light, for it was not by chance, but as the result of a train of reasoning, erroneous it is true it has since proved, that the discovery was made. Bernard observed, in the course of his physiological experiments, that on irritating the centres of the nerves connected with the salivary and lachrymal glands, an increased flow of their secretion was excited. Now, the liver derives some filaments from the pneumogastrics, and it occurred to him that irritating the centres of these nerves might excite the supposed glycogenic function of the liver into increased activity, and so lead to an augmented production of sugar, resulting in glycosuria. In his very first experiment he succeeded in obtaining the looked-for result, although, strangely enough, he discovered afterwards that the train of reasoning which had led him to it proved to be unfounded. The pneumogastrics, he ascertained, did not play the part of efferent nerves, or assist in the production of the effect, by serving to transmit an impression downwards. By dividing the pneumogastrics, and galvanising the lower or peripheral ends, he only obtained a negative result as regards diabetes; whilst the application of galvanism to the upper or central ends was followed, he states, by the production of saccharine urine. The galvanism, in the latter case, he looked upon as acting upon the centre of the pneumogastrics, and producing an influence which, like that arising in the experiment of puncturing the fourth ventricle, was transmitted down through the spinal cord and splanchnics to the liver.

This experiment of Bernard, of puncturing the medulla oblongata, was soon repeated, and his statement confirmed by others. The part of the medulla oblongata in which the puncture must be made to obtain a successful result is an exceedingly limited one, and many experiments may be performed without the effect that is looked for being produced, owing to the nicety and dexterity required in hitting the exact point. When the puncture, however, has been properly made, the urine in the space of an hour, or even in less time than this, will be found to have acquired a strongly saccharine character. The effect thus produced, it must be observed, is only of a temporary nature, the saccharine condition of the urine rarely lasting as long as, and never exceeding in duration, a few days. Bernard, believing that the result was due to an exaltation of the supposed glycogenic function of the liver, considered that it added another link to the chain of evidence he had adduced in support of his doctrine of glycogenesis. Another explanation, however, must now be offered; and this will form the subject of consideration a little further on.

It may be mentioned, *en passant*, that Bernard enumerates three effects as capable of being produced upon the urine—namely, glycosuria, polyuria, and albuminuria—by puncture of the medulla oblongata, according to the exact spot that happens to form the seat of lesion; and adds that, although these effects may be conjoined, still they may occur singly, showing their independence of each other. He states that when the puncture is made in the median line of the fourth ventricle, midway between the origins of the pneumogastric and auditory nerves, both glycosuria and polyuria are produced; that when the puncture, on the other hand, is made a little higher up, the urine is less abundant and less charged with sugar, but found often to contain albumen; and that when it is made a little below the origin of the auditory nerves, there is an augmentation in the quantity of urine without the passage either of sugar or albumen.

After division of the spinal cord, I have not found that saccharine urine has been produced, as after section of the medulla oblongata. When the division is practised below the origin of the phrenics, the animal retains the power of breathing, and life may continue for some time. Divided above the origin of the phrenics, however, death, unless artificial respiration immediately ensues, should be performed on account of paralysis of the diaphragm as well as the other muscles of respiration being induced. Now, I have divided the spinal cord as high up as between the second and third cervical vertebræ; and, upon afterwards keeping up the circulation by the performance of artificial respiration, as after division of the medulla oblongata, have failed to notice that any sugar has appeared in the urine.

It is asserted by Schiff, however, that glycosuria may be produced by introducing a needle into the spinal cord before and behind the origins of the nerves of the brachial plexus, and effecting a certain amount of destruction. The same result, according to this authority, may also be induced in frogs and rabbits by dividing the posterior columns of the cord; and a permanent diabetes, in rats—animals, it is stated, which easily bear the operation and may live from thirteen to seventeen days after it—by complete division of the anterior and lateral columns. Diabetes, further, says Schiff ('Journal de l'Anatomie et de la Physiologie,' 1866, p. 376), is well marked, and exists a long time, sometimes for whole weeks, after a transverse section of the spinal cord, if after this operation the lowering of the temperature of the animal is prevented, and the amyloid substance of the liver is not made to disappear by the supervention of high traumatic fever.

I have conducted some experiments for the purpose of ascertaining if separating the cerebrum from its connection with the medulla oblongata and spinal cord would produce glycosuria. Such an operation is of a nature calculated to lead incidentally to a serious disturbance of the functions of circulation and respiration —conditions that would have the effect by themselves of giving rise to a positive result. It may be stated, however, that I have succeeded in effecting a complete separation of the cerebrum from the parts below, without any sugar appearing in the urine. Amongst the experiments I have performed on this point, in the one where the least complication existed the animal lay in a quiet unconscious state with the breathing and heart's action continuing freely. The urine in an hour and a quarter's time after the performance of the operation was found to be quite devoid of sugar. Dissection showed that a complete separation of the cerebrum had been made, just above the pons varolii. The section passed through the crura cerebri, and permitted the cerebrum to be lifted away, leaving the cerebellum, pons varolii, and medulla oblongata together below.

Looking at the results of these various experiments, the inference to be drawn is that from the medulla oblongata an influence arises which, in some manner or other, affects the position of the amyloid substance contained in the liver; and further, that the medulla oblongata enjoys a power in reference to this matter which is not possessed either by the cerebrum or medulla spinalis. Regarding, then, the medulla oblongata in the light of a centre exercising an influence over some of the operations going on in the liver, it seemed to me important to endeavour to find out the channel by which this influence was transmitted. Now, it was whilst engaged in prosecuting this inquiry that I came down upon the fact that a strongly saccharine state of the urine rapidly followed injury or division of certain portions of the sympathetic system.

In starting out upon this investigation I first premised that the transit of the influence could not be—at least exclusively—either through the spinal cord or pneumogastrics, as division of each had been frequently practised without producing glycosuria. The effect of dividing both together, however, had not, as far as I was aware, been ascertained. I therefore commenced with the performance of this experiment, and found that no appearance of sugar in the urine was occasioned. In the experiment that was conducted the spinal cord was divided between the third and fourth cervical vertebræ, which necessitated, of course, the employment of artificial respiration in order to keep the circulation maintained.

This experiment, then, showed that division of the spinal cord and pneumogastrics together did not give rise to any production of sugar, as far as was to be judged of from the state of the urine. After decapitation, however, an operation necessarily securing a division of all the nerve-structures passing through the neck, an opposite result was obtained, a strongly saccharine condition of the urine being in the course of a short time discoverable. As in the previous experiment, artificial respiration, of course, required to be performed to keep the circulation maintained.

The results thus far yielded naturally led me, in the next place, to give attention to the sympathetic. Where the operation had been such (namely, where decapitation had been performed) as to leave no possibility of any influence being transmitted from the medulla oblongata to the liver, a production of sugar occurred which led to a strongly saccharine condition of the urine being encountered. Where, on the other hand, division of the spinal cord and pneumogastrics only had been effected, no such result was observed. Experiment had now to be appealed to to determine if the sympathetic filaments passing through the neck formed the channel of communication sought for.

Division of the carotid sympathetic, or that portion of the sympathetic system which passes down from the superior cervical ganglion to the chest in front of the vertebral column, constitutes an experiment that had repeatedly been performed by physiologists, on account of the interesting and instructive effect it produces in reference to animal heat. Nothing had been noticed about it with respect to sugar, and upon performing it, with special attention directed to this point, it was not found to be followed by any production of saccharine urine.

But there is another portion of the sympathetic running through the neck, the effect of division of which remained to be ascertained. The filaments accompanying the vetebral artery constitute the portion to which I refer. This I now determined to subject to experiment, and thus I was conducted to the discovery of the fact that by operating upon certain parts of the sympathetic system an artificial diabetes may be produced. A paper entitled "Lesions of the Nervous System producing Diabetes," to be found in the 'Guy's Hospital Reports' for 1859, contains a full account of the experiments that I have performed upon this subject.

In my first experiment upon the vertebral sympathetic I succeeded in rapidly producing a strongly saccharine state of the urine. To give some particulars regarding the results obtained, I may state that I have a record before me of an instance in which the filaments were divided on both sides of the neck, between the superior thoracic ganglion and the vertebral canal. In half an hour's time the urine presented a strongly saccharine behaviour. In another experiment the filaments on one side of the neck only were at first divided. The urine, in an hour and a half's time, was found to contain only traces of sugar. The filaments upon the other side were now divided, and in half an hour's time the urine was observed to have acquired a strongly saccharine character.

It may be mentioned incidentally, that division of these particular filaments is invariably attended with the production of fatal pleurisy. The inflammation evidently results from the injury inflicted on the sympathetic, and not simply from the seat of operation being in close contiguity to the pleura; because when it has happened, as has sometimes been the case, on account of the difficult nature of the operation, that the filaments have escaped being divided, no pleurisy has resulted, although the circumstances have otherwise stood the same as far as regards the injury inflicted in the neighbourhood of the pleura.

I afterwards found that glycosuria could be produced by operating upon other parts of the sympathetic, besides the vertebral filaments. Divisions of the carotid sympathetic in its course through the neck does not, as has been mentioned, give rise to glycosuria; but by removal or injury of the ganglion above—that is, the superior cervical ganglion—the urine may be made to acquire in a very short time a strongly saccharine character. In illustration of this assertion, the particulars of an experiment may be furnished, in which I first of all removed the ganglion on the right side only. The urine in an hour's time was found to be strongly charged with sugar. As a result of the operation, it was also noticed that the ear belonging to the side on which the ganglion had been removed, was 3° Fahr. warmer than the other, the pupil more contracted, and the nostril drier. On the following day the urine still presented a saccharine behaviour. On the third day, however, the sugar had disappeared. On the fourth day, the urine being ascertained to be free from sugar, the ganglion on the other side was removed. In half an hour's time the urine had again acquired a strongly saccharine character.

In a couple of other experiments a quantitative determination of the sugar appearing in the urine was made, and the following results obtained. In each of these experiments both the ganglia were removed. In one of them the urine, half an hour after the operation, was found to contain 20·5 grains of sugar to the fluid ounce; and an hour and a half later, 11·4 grains. In the other it contained 22·86 grains to the ounce an hour and twenty minutes after; and 34·08 grains half an hour later.

I have also operatedupon the sympathetic in its course through the chest; but here, it must be remarked, a considerable want of uniformity has been noticed in the results obtained upon different occasions. Its division has sometimes been quickly followed by the appearance of a large quantity of sugar in the urine. At other times, however, only traces of sugar have been discoverable; and, at other times, again, none at all. I have not found that division on both sides has been more frequently followed by a diabetic effect than division on one side only; nor have I been able to discover that the result has been influenced by the particular part of the thoracic sympathetic that has happened to form the seat of operation.

According to what I have seen, glycosuria is less readily produced by these operations upon the sympathetic in the rabbit than it is in the dog. I have noticed, it is true, glycosuria ensue upon removing the superior cervical ganglion in the rabbit but not with anything like the rapidity, or to the marked extent, that I have seen it occur in the dog. As regards the vertebral filaments of the sympathetic, I have not succeeded in satisfactorily exposing and dividing them in the rabbit, on account of their minuteness and depth. It is an operation that, even in the dog, is attended with a considerable amount of difficulty.

As with the puncture of the medulla oblongata so with these experiments on the sympathetic, the glycosuria produced is only of a temporary nature.

Having noted the fact, the question next comes—how is it that glycosuria is thus produced by these several operations upon the nervous system? I have mentioned the idea that led me to experiment upon the sympathetic in connection with glycosuria. The medulla oblongata seemed to exert an influence over the amyloid substance contained in the liver, and I looked for the channel by which this influence might be transmitted downwards. The fact that glycosuria is producible by lesions of certain parts of the sympathetic was thus brought to light, but I do not now consider that the train of reasoning which led me to it was correct. Looking at the whole of the evidence that has been obtained upon the point, I must own I do not think that the glycosuria produced by operating on the sympathetic can be legitimately assigned to a simple interruption of the transmission of nervous influence from the medulla oblongata to the liver. It may be considered that this conclusion is strongly supported by the fact that division of the nerves proceeding to the liver in the lesser omentum is not found to be followed by glycosuria. After carefully isolating the hepatic artery, portal vein, and hepatic duct, I have divided all the remaining structures in the lesser omentum, including, therefore, the nerves passing to the liver, without observing any appearance of sugar in the urine. The sympathetic has been shown by modern physiological research to be capable of modifying the circulation through a part by the influence it exerts upon the muscular coat of the arteries. Now, the most reasonable conclusion that can be arrived at is, that it is in this direction that we must look for an explanation of the production of glycosuria through the medium of the sympathetic.

In my first experiments upon the sympathetic I invariably, or almost invariably, succeeded in producing artificial diabetes by the destruction of the superior cervical ganglia. Later, however, on repeating the experiment, I was surprised, and for some time puzzled, upon finding that I could not reckon on obtaining the effect that I had been able so readily and so constantly to produce before. There could be no doubt about the presence of the sugar in my early experiments, for quantitative examinations of the urine, as already mentioned, were made, and amongst the results obtained no less than 34 grains of sugar to the fluid ounce were upon one occasion met with within two hours after the operation.

To what, then, could this difference be attributable? I was not conscious that there was any difference in my mode of operating, but still there was the difference as regards the result. Whilst reflecting upon the matter, it occurred to me to try the effect of using another anæsthetic in the place of chloroform during the performance of the operative part of the experiment. I was induced to do this on account of its having been noticed by Bernard that chloroform, like galvanism, exerts a counteracting influence upon the effects produced upon the circulation and temperature by section of the sympathetic.

It is found, for instance, that on destroying the superior cervical ganglion, or dividing the connecting cord between it and the ganglion below, the vascularity of the corresponding side of the head is increased; and that with this increased vascularity there is an increase in the temperature of the parts. The rabbit forms a convenient animal for showing this result. Suppose, then, a rabbit to have formed the subject of experiment, the ear will be found to be conspicuously more vascular, and sensibly to the touch, as well as by the indications of the thermometer, decidedly warmer on the side of the operation than on the other. There will also be a marked disparity observable in the size of the two pupils: that on the side of the operation being very much smaller than the other. Now, upon galvanizing the upper portion of the divided sympathetic all these phenomena will be found to disappear; and not only this, but exactly the converse condition will be produced, that is to say, the vascularity and temperature will fall below what is natural, and the pupil become larger than the other.

The inhalation of ether and chloroform has been observed by Bernard to occasion the same reversal of the effects produced by division of the sympathetic as the employment of galvanism. As insensibility becomes established, the ear becomes paler, and its temperature lower. Upon reviewing these facts, it occurred to me that a similar counteracting influence might be exerted by chloroform upon the effect producible by division of the sympathetic upon the urine, and I therefore resolved to perform the experiment under the anæsthesia produced by puff-ball instead of chloroform. The fumes of burning puff-ball, it may be remarked, whilst producing anæsthesia, act in a different manner from chloroform upon the circulation; for whilst the latter weakens in a striking manner the action of the heart, and diminishes the tension of the arterial system, no such results are produced by the former. I have now several times performed the experiment of destroying the superior cervical ganglion whilst the animal has been under the anæsthetic influence of the smoke of puff-ball, and have invariably observed a rapid production of strongly saccharine urine.

I do not remember for certain whether I used chloroform in my first experiments to an extent to produce so full an anæsthetic effect as I am now accustomed to do; but I am inclined to think that I did not; at all events, this is the only way in which I can account for formerly succeeding in producing a marked glycosuria, and subsequently obtaining only a slight diabetic effect, if any diabetic effect at all. Under the use of puff-ball, as has been remarked, the operation on the ganglion has always been attended with the production of strongly saccharine urine.

Looking upon the phenomenon of glycosuria in these experiments as resulting from the effect produced on the circulation, the question suggests itself—is it due to an augmentation in the vascularity of the liver, like that which occurs in the ear? This is a question which happens readily to admit of being answered by experiment; and from the experiments that I have performed a direct reply can be given. I have ligatured the hepatic artery, and have still found that saccharine urine has been produced by destruction of the superior cervical ganglion of the sympathetic. The result obtained from a quantitative analysis of the urine showed that, an hour after the operation, it contained 8½ grains, and two hours after, 12 grains, of sugar to the fluid ounce. I have likewise ligatured the cœliac axis, and have afterwards also found that sugar to nearly the same extent has appeared in the urine. In an hour's time, for instance, the urine was observed to contain 7·38 grains, and two hours' later 6·66 grains, of sugar to the fluid ounce. The further experiment has also been performed of ligaturing the portal vein as well as the hepatic artery, before the destruction of the ganglion. In this experiment, as was to be expected, there was no appearance of sugar in the urine.

It is thus rendered evident that the saccharine urine produced by operating upon the sympathetic cannot be attributable to a direct influence exerted on the arteries of the liver. In the parts which show an increased vascularity as the result of the operation, the effect is due to a paralysis of the muscular coat of the arteries. Through this paralysis the vessels yield to the pressure of the blood within, and so the dilatation that occurs is explained. Now, if the production of sugar were due to an implication of this kind affecting the arteries of the liver, *i. e.* to an increased vascularity of the liver arising from paralysis of its vessels, it is not consistent that glycosuria should be observed after the application of a ligature to stop altogether the arterial supply to the organ.

Schiff ('Journal de l'Anatomie et de la Physiologie,' Paris, 1866) assigns the development of a ferment in the blood as the cause of artificial diabetes produced by the operations on the nervous system that have been referred to. He says that as far back as twenty years ago he had shown that lesion of the nervous centre in the region which forms the seat of operation in Bernard's puncture was accompanied with a dilatation of the small vessels of the intestine and liver, producing a kind of paralytic hyperæmia of these organs. He considers that from this hyperæmia a ferment is developed in the blood which constitutes the cause of the appearance of sugar that takes place. It is not essential, he believes, however, for the production of glycosuria, that the circulation of the liver should be involved—in other words, that this organ should form the seat of hyperæmia, hyperæmia of sufficient extent existing elsewhere sufficing, he considers, for the development of the requisite amount of ferment to determine the result. "Le diabète," says Schiff, "par suite de l'hypérémie pourrait donc bien ne pas être l'effet spécifique d'une hypérémie du foie, mais de chaque hypérémie générale d'une certaine étendue."

The question regarding the production of glycosuria by the development of a ferment in the blood from an arrest of the circulation has already formed the subject of discussion. My own experiments do not support the view of Schiff in the shape he has propounded it. I believe glycosuria may be connected with an alteration in the quality of the blood, and expressed this opinion in the 'Medical Times and Gazette,' of June 3rd, 1865, in the following words :—"With these experiments I do not see how it is reconcilable that the effect of the operation on the sympathetic can be in a direct manner attributable to an action upon the blood-vessels. It is only upon the coats of the arteries that we can conceive the sympathetic to exert any material direct influence, it being through the muscular element that it influences the circulation. Possibly the operation on the sympathetic may lead to an alteration in the quality of the blood that is passing to the liver, and so occasion the result. This is the most likely supposition that I can offer at present."

That the condition of the blood has to do with the result is confirmed by the effect of introducing carbonate of soda into the circulation, previous to operating upon the sympathetic. The injection of 200 grains of this agent, dissolved in a small quantity of water, into the jugular vein before the removal of the superior cervical ganglion, suffices to prevent an appearance of sugar in the urine. This experiment I have several times performed, and always with the same result. The urine has remained perfectly devoid of sugar; and this, after the employment of puff-ball as an anæsthetic.

It has already been mentioned that the introduction of phosphoric acid into the circulation leads to the production of glycosuria, and, as might be expected, a saccharine condition of the urine is also encountered when the injection has been conjoined with the removal of the superior cervical ganglion. In an experiment of this kind, where the urine was subjected to a quantitative examination, it was found to contain 7·3 grains of sugar to the fluid ounce an hour and a half after the operation.

It may be looked upon as probable that the glycosuria produced by puncture of the floor of the fourth ventricle is due, like that resulting from the operations referred to on the sympathetic, to an influence exerted upon the circulation. The researches of Bernard showed that the effect of the puncture was not occasioned by an influence transmitted to the liver, either through the pneumogastrics or splanchnics; for these nerves had been divided, and still an appearance of sugar in the urine had taken place. Division of the spinal cord, however (the division, of course, required to be made below the phrenics, for respiration, and hence life, to continue), was found to arrest the production of glycosuria. Now, the operation of puncturing the fourth ventricle has been observed to be followed by an exaltation of the abdominal circulation, and division of the spinal cord happens to induce exactly the reverse. By division of the spinal cord the activity of the circulation of the abdominal organs is found to be lessened, and the temperature lowered. In this way, therefore, division of the spinal cord exerts a neutralizing effect upon that of puncturing the fourth ventricle; and, looking upon the circulation as the medium through which glycosuria resulting from puncture of the fourth ventricle is produced, the non-appearance of sugar in the urine after division of the spinal cord tallies with what might be looked for.

The question comes now: how do all these experimental considerations bear upon the disease in question, as it occurs in the human subject?

It has been shown that even in a state of health the power we possess of disposing of the saccharine element of food is not an unlimited one; in other words, that when ingested beyond a certain amount, and especially at a period of fasting, when absorption is more rapid than at other times, sugar appears in the urine, showing that all has not undergone the process of assimilation. Now, some cases of diabetes seem to consist simply of a want of the proper amount of assimilative power over this element of food. The quantity of starch and sugar which can be assimilated by the healthy subject fails to be equally susceptible of being disposed of by the diabetic person : and thus, the saccharine condition of the urine that ensues when an ordinary mixed diet is consumed. Cases are not uncommon, especially amongst elderly people where, under an exclusion of starch and sugar from the food, the urine entirely loses its saccharine character, and the symptoms of diabetes disappear. Indeed, as stated above, all the error that seems to exist is a want of power to apply these principles to the purposes of life. From this want of power the sugar fails to undergo the changes that it ought to do to fit it for service in the economy; and, as a consequence, it reaches the general circulation, and thence appears in the urine. Its presence in the circulation gives to the blood an unnatural condition, and in this way, it may be considered, the symptoms experienced by the patient are produced. By excluding the saccharine element from the food, and thus making no demand upon the function which is at fault, the circulating fluid is restored to a natural state, and the symptoms of diabetes disappear. Under such circumstances the diabetic is to all intents and purposes in the position of a healthy person, as far as the performance of the functions of life generally is concerned.

Barring the want of assimilative power over the saccharine element of food, no difference in reality is to be discerned between such a diabetic and a healthy individual. So long as the defective power is not taxed, nothing amiss is to be perceived; for it is not essential that this element should enter into the constitution of our food. Out of the other elements we can obtain all that is requisite for the support of life. To repeat: the only difference between such a diabetic and a healthy individual is with reference to the power of appropriating starch and sugar. In the case of the healthy person these elements, when ingested, are assimilated and applied to the purposes of life. Not so, however, in the case of the diabetic. Here, failing to be properly assimilated, these elements lead to an appearance of sugar in the general circulation, and thence its discharge with the urine.

In illustration of the type of the complaint that has just been alluded to, I may give the report of a case which stood in the Appendix of Cases in the first edition of this work; but cases of this kind are by no means of uncommon occurrence. The patient, as long as he is kept upon a diet free from saccharine and amylaceous materials, passes no sugar; but as soon as these are taken, sugar appears in the urine. Under the influence of dietetic and medicinal treatment, however, such an improvement may, in the course of time, be often brought about in the case, as to allow of a certain amount of starch and sugar being ingested without any sugar appearing in the urine.

James B—, a patient aged 57, sent to me from the country, and admitted under my care into Guy's Hospital. Had been the subject of diabetes for about nine months previous to admission, and at one time the quantity of urine passed amounted to about six quarts a day. Formerly he had suffered in a pretty severe manner from the usual symptoms of the complaint, but latterly the urgency of his symptoms had somewhat subsided. His case was one of uncomplicated diabetes. The following Table furnishes a representation of the patient's progress whilst under observation in the Hospital:

Date.	Quantity of urine passed per 24 hours in oz.	Sp. gr. of urine.	Quantity of sugar per oz. of urine in grs.	Quantity of sugar passed per 24 hours in grs.	Diet and medicine.
Sept. 2nd .	85	1039	44·40	3774	Full mixed diet; sherry ℥vj. Pulv. Opii gr. j ter die.
,, 3rd .	94	1040	44·40	4173	
,, 5th .	82	1039	46·15	3784	
,, 6th .	50	1036	28·90	1445	Animal diet, consisting of 1 chop, 1 lb. of dressed meat, and 3 pints of beef tea; with an allowance of greens for dinner. Brandy ℥v. Pulv. Opii gr. j ter die. Jul. Rhei co., Jul. Ammoniæ, āā ℥ss ter die.
,, 7th .	66	1018	3·33	219	
,, 8th .	94	1018	4·13	388	
,, 9th .	86	1020	Trace of sugar		
,, 10th .	54¼	1022	Trace of sugar		
,, 11th .	51	1019	No sugar		
,, 12th .	63	1010	No sugar		
,, 13th .	63	1015	No sugar		
,, 14th .	108	1009	No sugar		
,, 15th .	69	1015	No sugar		
,, 16th .	60	1017	No sugar		
,, 18th .	92	1012	No sugar		
,, 19th .	54	1019	2·18	117	Same diet as above, with the addition of 2 oz. of bread. Medicine as before.
,, 20th .	74	1016	2·66	196	
,, 21st .	91	1017	2·35	213	The bread omitted. Diet and medicine otherwise as before.
,, 22nd .	100	1023	5·71	571	
,, 23rd .	61	1020	3·87	236	
,, 24th .	57½	1022	1·60	92	
,, 25th .	86	1014	No sugar		
,, 26th .	72	1013	No sugar		
,, 27th .	88½	1017	No sugar		
,, 28th .	87½	1014	No sugar		
,, 29th .	84	1014	No sugar		Same diet, with the addition of 2 oz. of bran biscuit.
,, 30th .	72	1015	No sugar		
Oct. 1st .	72	1017	No sugar		Same diet, without the bran biscuit.

It will be seen from the above tabulated report that under the hospital full mixed diet the patient passed about 4000 grains of sugar a day. Upon being placed on a diet from which starch and sugar were excluded, the quantity fell until on the fourth and fifth days there were traces only present, and on the sixth day none. After continuing in this way for several days, two ounces of bread per diem were for a couple of days allowed. Sugar immediately showed itself in the urine, and, although the bread was then taken off, it continued during the following two days, increasing in amount. It then declined, and after two days more disappeared altogether. The urine passed on the 4th and 17th of Sept. was not examined, and thus it is that these two days are missing from the report.

It is necessary to be aware, in order to avoid being led into giving an erroneous opinion and creating disappointment, that there are many diabetics going about who belong to the type of case represented above, and who are keeping their urine free from sugar by pursuing a restricted diet. Such a case may happen to fall under the notice of a medical man, and the opinion may be given, without full inquiry into all the circumstances connected with it, that no diabetes exists. The patient, perhaps, is told that he may resume an ordinary diet, and in the course of a short time he finds all his old symptoms returning, and is thus made aware that his hopes have been falsely raised. He is obliged to be informed that he must go back to his former dietary scheme, which very likely he will take to less kindly now than he did before. If a guarded opinion had been expressed, and he had been desired to partake only for a day or so of an ordinary mixed diet, and an examination of the last specimen of urine passed before going to bed (I name this specimen because if sugar at all be passed it will be almost sure to be present in this) had been made, the real state of the case would have at once been disclosed. Thus, from looking simply at the fact that a person may be passing urine free from sugar, it must not be concluded, without the question of diet being taken into consideration, that no diabetes exists.

In exemplification of what has been said, the following case may be mentioned. A patient, who had been under the care of the late Dr. Camplin, came to consult me about himself. According to his account he had been suffering from diabetes for about a couple of years, but he did not present the ordinary aspect of a diabetic, being exceedingly stout, nor did he experience any of the usual symptoms of the disease. The urine he was passing was normal in quantity, of a natural colour, turbid from the deposition of lithates, and perfectly free from sugar. If I had not known by whom he had been told that he was labouring under diabetes, I should have felt inclined to have questioned the fact. I ascertained next, that he had been scrupulously confining himself to a restricted diet; and in order to be enabled to form an opinion upon what I had to deal with, I desired him to partake moderately of ordinary bread at his meals for a day, and to bring me a portion of the urine that was passed the last thing before going to bed. This he did, and upon its being tested a large quantity of sugar was found to be present. The morbid state, therefore, still existed, although no evidence of it was perceptible as long as the function at fault escaped being taxed.

Other cases may be encountered in which even a less degree of defective power than what has been referred to exists; the capacity for assimilating the saccharine element of food not being lost altogether, but existing to an extent below what is natural. In these cases a certain amount of starch and sugar, varying in different instances, may be consumed without causing the urine to present a saccharine behaviour; whilst if this quantity be exceeded, an appearance of sugar will be immediately observed. A certain amount of assimilative power over the saccharine element exists, but not an amount equal to what is natural. This type of case, therefore, furnishes us with an illustration of the existence of a less extent of deviation from the healthy condition than that which has just above been alluded to.

As regards the amount of starch and sugar that can be ingested in the class of case under consideration without giving rise to a saccharine condition of the urine, a great degree of variation is in different patients to be noted. In the same patient also a difference exists at different periods and under different circumstances. For instance, a patient when first falling under treatment may be passing sugar notwithstanding the strictest exclusion of starch and sugar from the diet. After a while it is found, first under the restricted diet, that the sugar disappears from the urine; and then, that a certain amount of food containing starch and sugar can be taken without giving rise to saccharine urine. The power of disposing of these elements may go on increasing until ultimately, in some cases, an ordinary diet can be consumed without giving rise to an appearance of sugar in the urine. This result, however, must rightly be spoken of as somewhat exceptional, for usually, when diabetes in a marked form has once set in, the power of assimilating the saccharine element remains throughout more or less impaired.

I will furnish the details of a couple of cases which will serve to illustrate the type of case under review. In one the disease, although at the beginning severe, was afterwards so far recovered from that an ordinary diet could be consumed without causing any appearance of sugar in the urine. Later, however, a relapse was suddenly brought on by an act of indiscretion on the part of the patient in drinking off a large quantity of cider; and it then took some time before the former improved state could be regained. The other case forms an example of an unusually mild form of the disease. An ordinary diet, which at first led to the return of a little appearance of sugar in the urine, was afterwards tolerated without any sugar being discoverable.

John W—, æt. 48. This person first fell under my care as an out-patient at Guy's Hospital in March, 1864. The account given at that time was that he had always enjoyed good health until two years previously, when he began to suffer from dryness of the mouth and an unquenchable thirst. From this time also, as he had noticed from the fitting of his clothes, he had been gradually losing flesh; and he had found by the scales that he had fallen about 2½ stone below his usual weight. His urine when he came to me was excessive in quantity, of high sp. gr., and loaded with sugar. He was placed upon the restricted diet, and ordered a mixture containing the bicarbonate of potash and some aromatic spirit of ammonia. Under these measures the urine soon lost its saccharine character, and in the course of a few months it was found that he could take a moderate amount of ordinary bread and potatoes without causing any re-appearance of sugar. In six months' time he had regained one stone of his lost weight, and was now consuming an ordinary diet without passing any sugar. He continued in this way for another six months, when he was tempted to take some cider, and drank off, according to his account, from a pint to a pint and a half nearly at a draught. Almost immediately afterwards he began to experience some of his old symptoms. He fancied at once that his complaint had returned upon him, and when he came to the hospital, a few days after, it was soon made evident that his suspicions were well founded. His urine was found to be loaded with sugar, and there were other indications showing that a sharp return of diabetes had set in. It took a couple of months before the sugar could be again made to disappear from the urine, although he returned and strictly adhered to the original plan of treatment that had been adopted. Subsequently he was able to resume an ordinary diet without passing sugar, but latterly, whenever I have examined his urine, I have always found a little. He has, however, the appearance of a man in the enjoyment of perfect health, and none of the ordinary symptoms of diabetes are present.

The other case to be described likewise occurred amongst my out-patients at Guy's Hospital. Outwardly there was no appearance of diabetes, and the patient had only been ill a few weeks. He had been told before he came to me that he was suffering from diabetes, for which he had been following a restricted diet. According to his account he had never passed an inordinate quantity of urine, nor had he experienced any particular thirst. His urine was examined and found to be perfectly devoid of sugar. He was thereupon recommended to try the effect of resuming for a short time an ordinary diet, and the urine he brought me in a few days' time yielded upon analysis an indication of being charged to the extent of 2·85 grains to the fluid-ounce with sugar. He was passing, he informed me, about four pints in the twenty-four hours, which, with the quantity of sugar mentioned as present per ounce, would give about 228 grains—but a small amount compared with what is met with in most cases—as the quantity of sugar voided during that period. He was now put back upon a restricted diet, and three days afterwards the urine contained only a trace of sugar. This trace subsequently disappeared; and, a fortnight then elapsing without any sugar having been passed, the patient was allowed a less exclusive diet. For a week his food consisted of about half a pound of potatoes, and the same quantity of bread per diem, with meat, fish, greens, coffee and tea. At the end of the week his urine was found to present no reaction of sugar. During the following week the allowance of bread and potatoes was doubled, and the urine still remained devoid of sugar. The next week beer was allowed in addition, and again the urine gave no indication of the presence of sugar. The patient, considering himself quite recovered, now ceased to attend, and has not fallen under my notice since.

As previously mentioned, it is especially amongst elderly persons that these more favorable forms of diabetes are met with. Age, according to my experience, forms an item of consideration of vast importance in reference to diabetes; and, contrary to what is noticeable in the case of most complaints, the older the subject, the less the severity that the disease assumes, and the more amenable is it to treatment. With a person, say over fifty, it is seldom that any anxiety need be entertained about the result if resolution enough be possessed to persevere in carrying out the measures that may be found to be required, according to the progress of the case, to keep the disease in abeyance. In some cases, amongst young subjects, it may be found, also, especially when the disease is taken early, that under the exclusion of starch and sugar from the food a disappearance of sugar takes place from the urine, although such a result is of infinitely less frequent occurrence in these than in those occurring amongst the more advanced in age. The slightest departure from a restricted diet, as a rule, in young subjects, suffices to bring back the sugar; and should the urine continue long in a saccharine state, the chances are that after a while the strictest attention will be found ineffectual in rendering it again devoid of sugar. The issue now must be considered doubtful, if even the prognosis can be pronounced as otherwise than unfavorable.

In another class of case, notwithstanding the strict exclusion of starch and sugar from the diet, sugar is still recognisable, and, it may be, in considerable quantity, in the urine. There is evidently in these cases something besides a defective assimilative power over the saccharine element of food. The origin of the sugar, however, may be here also referred to a faulty action connected with the liver. Amyloid substance is formed in the organ in the absence of the ingestion of starch and sugar, and a downward metamorphosis of this amyloid substance into sugar will account for the saccharine state of the urine that may be observed under a restricted diet.

It is chiefly amongst young and middle-aged subjects that this form of the disease is encountered. The bearing of age on the severity of the complaint has just been alluded to. It has been stated that the most controllable cases are those occurring in elderly subjects. In young subjects it sometimes happens that the sugar may disappear from the urine under the exclusion of starch and sugar from the food, but often, it must be said, this fails to be observable. Being less susceptible of control, these cases are of a correspondingly more serious nature. However rigidly the dieting may be carried out, the patient still continues to pass sugar. Should the quantity happen not to be great, the symptoms of the disease will be subdued, and life may be carried on without any material evidence of disturbance; but should the circumstances be otherwise, simply a mitigation of the symptoms will be perceived, and ultimately an unfavorable issue may be looked for.

In these cases, where sugar continues to be discharged under a restricted diet, the amount passed forms an index of the severity of the disease, or the intensity of the morbid state existing, which varies considerably, not only in different cases, but at different periods in the same case. It is the same here as it is with the other forms of the complaint—the disease is met with exhibiting very different degrees of intensity.

Upon a given diet, whether restricted or not, a considerable range is observed in the quantity of sugar passed, the intensity of the disease varying accordingly. Taking a particular case, anything, it is found, that produces a disturbing influence upon the system aggravates the diseased condition that prevails, and causes the quantity of sugar passed to become greater. By treatment, such an amelioration, on the other hand, may often be produced that an increased assimilative power is acquired.

It has been previously shown that glycosuria is experimentally producible by injuring certain parts of the nervous system. Now, cases can also be brought forward, from which it may be concluded, that with diabetes occurring in the human subject, the nervous system is frequently at the least, if nothing more, at the bottom of the disease. It has been contended that the origin of the sugar must be referred to a perverted action connected with the liver, and evidence can be adduced to show that this perverted action is sometimes distinctly traceable to a cause originating in the nervous system. Such, I think, will be conceded from what I am now about to set forth.

After Bernard made known that artificial diabetes could be produced by puncturing the medulla oblongata, pathologists looked to this part in search of evidence of disease that might account for human diabetes. Although careful examination has repeatedly been made, nothing has been discovered to support the idea that Bernard's experiment suggested. If disease of the medulla oblongata in particular, however, has not been discovered, cases have frequently happened in which injury to or disease of some part or other of the brain has evidently been connected with the origin of the complaint. I remember a case in which an intense form of diabetes immediately followed a violent blow upon the head. The subject of the case was a cadet at Sandhurst, of about twenty years of age. Whilst going through his military exercises he happened to receive a violent blow upon the head from the ramrod of a piece of artillery, which knocked him down and rendered him unconscious for a short while. He recovered from the blow, and went about in an ordinary manner; but, a few days after, symptoms of diabetes of a strongly marked character set in. There was nothing to lead to the suspicion that the disease had previously existed; on the contrary, he had been up to the time of the accident in the enjoyment of perfect health. Shortly after the accident this patient fell under my own notice, suffering in a very severe manner from the disease.

Bernard remarks that falls upon the head have been known to be followed by diabetes, and directs attention to a case in which a quarryman became diabetic in this way. The sugar, it is recorded, disappeared from the urine as recovery from the injury to the head took place.

In the following case, which occurred within my own experience, sugar was found in the urine a few hours after a fatal injury to the head had been sustained. A little girl, four years of age, had been run over in the street and was brought into Guy's Hospital. She lived four and a half hours after admission. During this time she lay in a state of quiet unconsciousness, without the power of swallowing. Her respiration was of a convulsive or sobbing but not stertorous character. A little blood ran from the nose and mouth. It was found after death that the skull had been fractured through the base, and that the surface of the base of the brain was slightly bruised. The fornix was slightly ecchymosed. Some ecchymosis was also observable upon the floor of the fourth ventricle from slight effusion of blood into the substance beneath. The ventricles contained a little bloody serum. A little blood was found on the outside of the dura mater, but the dura mater itself was not injured. The urine removed from the bladder at the post-mortem examination was tested and found to contain sugar. A quantitative analysis was subsequently made, and 5½ grains of sugar to the fluid-ounce formed the amount that was discovered to be present. The urine was also in a slight degree albuminous.

In the 'Archives Générales de Médecine,' t. xx, 1862, Fischer has placed together a number of cases gathered from various sources in which diabetes followed traumatic lesions of the brain. In twenty-one cases thus collected it appears that four consisted of polyuria without glycosuria (diabetes insipidus), three of polyuria with slight glycosuria, six of temporary glycosuria, and the remaining eight of permanent glycosuria or confirmed diabetes mellitus. Arranged according to seat of injury, six resulted from blows upon the forehead, five from blows on the top and sides of the head, and five from blows on the occiput. In the remaining five the seat of injury was undetermined.

Diabetes has also been known to follow, and it may be fairly assumed as an effect, lesions of the brain resulting from disease. A case was mentioned to me by my former colleague the late Dr. Barlow, in which diabetes supervened upon cerebral disease attended with hemiplegia. The patient, an alderman of London, was under Dr. Barlow's observation from the beginning. Shortly after the hemiplegia showed itself, strongly marked diabetes became developed. No symptom of the disease had been apparent before, and the urine, upon being tested, as it happened to be, when the patient was first attacked, was found to be free from sugar.

The particulars of another case closely resembling the above were communicated to me by Dr. Gull, under whose notice the patient fell. A member of the medical profession, at the age of fifty-two, was seized with a fit of apoplexy. Recovery from the fit took place, but hemiplegia of the left side remained. Five weeks after the seizure occurred the patient, who had never previously experienced any symptoms to lead to the suspicion of diabetes existing, began to undergo rapid emaciation. This led to an examination of the urine being made, which resulted in the disclosure that it was loaded with sugar.

Mental influences are also, I am firmly of opinion, capable of leading through the nervous system to the production of diabetes. I have seen several cases which I believe have originated in worry of mind, anxiety, or over mental work; and I have often observed in patients suffering from the disease that these influences have produced a sensible increase in the amount of sugar discharged—indeed, my experience leads me to look with confidence for an aggravation of the complaint under exposure to the influences named. As bearing upon this point, I may state that a case is mentioned as having been seen by Rayer, in which the disease succeeded a violent fit of passion.

The following case I look upon as one in which a temporary diabetic condition was evidently occasioned by a state of mental excitement. In January, 1867, a middle-aged gentleman was brought to me by his medical adviser in consequence of symptoms of diabetes having recently shown themselves. He had latterly been suffering from great nervous excitement. Without any just cause everything looked black and gloomy before him, and he had become so completely unnerved as to be unfit for properly attending to the duties of his profession. I saw him upon several occasions, and each time found that the urine was charged with sugar. It was not an ordinary well-marked case of diabetes, but upon one occasion I found as much as fifteen and a half grains of sugar to the fluid ounce of urine; and this, notwithstanding that a partially restricted diet was being followed out. He was advised to give up all professional engagements for a time, and go right away from London. This he did, and in the course of a few months returned completely restored in every way. A year and a half afterwards I chanced to meet him in the street, and found him looking the picture of health. At my request he forwarded me a specimen of night and morning urine to examine for sugar, and in the case of both an absence of saccharine behaviour was encountered. As regards eating and drinking, he informed me he was living like other people, or precisely as he had formerly been accustomed to do, with the sole exception that he had left off taking sugar in his coffee and tea. The attack of glycosuria that I have referred to was the second that had come on under similar circumstances.

Morbid anatomy has contributed nothing towards elucidating the pathology of diabetes. We refer the origin of the sugar encountered in the disease to a faulty action of the liver, but there is no structural change of this organ to be discovered, as there is for instance in the case of the kidney under the existence of albuminuria. We have a manifestation of a disordered functional action to deal with without any discernible anatomical alteration to account for it.

Various morbid appearances are met with, but these constitute only effects, and do not therefore essentially belong to the disease. Disease of the lungs for instance, assuming the character of phthisis, forms one very common concomitant of diabetes, and one by means of which the patient is not unfrequently carried off. This disease of the lungs is commonly spoken of as phthisis; but although it runs the same course and produces the same symptoms as ordinary tubercular phthisis, yet it may be considered as constituting, certainly as a rule, a different affection, being due to simple inflammatory action instead of dependent upon the deposition of tubercle. It is true pathologists are not all agreed upon what is to be defined as tubercle. What some consider as little masses of grey hepatized lung proceeding from common inflammation, the pneumonic phthisis of Dr. Addison, others regard as tubercle. Now, such is the kind of disease which specially accompanies diabetes. It is a simple inflammatory affection, and may occur in previously healthy persons as a consequence of exposure to cold. The proneness in diabetes to its invasion may be regarded as dependent upon the morbid condition which the blood has acquired by virtue of the presence of sugar; for, if the sugar be kept down by treatment, my experience is that the susceptibility in question no longer exists, and if the diabetic be carried off it will in all probability be in some other way. Like the inflammation set up by tubercle this form of disease leads to a breaking down of the lung-tissue, and the formation of cavities.

Of course I do not mean to deny that true tubercle may become developed and constitute the cause of pulmonary disease in the diabetic ; but what I contend for is, and this agrees with the extensive experience in morbid anatomy of my colleague, Dr. Wilks, that the ordinary condition met with is one resulting from simple inflammatory action without any accompanying tubercle.

ETIOLOGY.

Not much can be said at present about the cause of diabetes. I have been often asked if intemperance is not a frequent source of the disease, but I cannot say that I have observed any connection whatever between the two, and do not believe that any exists. Prout thought that, in many instances, he had been able distinctly to trace diabetes to exposure to cold; or sometimes to rheumatic attacks brought on by exposure to cold and moisture. It is possible that this idea of Prout may be correct, but my own experience has not afforded anything to confirm it.

I have already alluded (p. 189 *et seq.*) to the connection that appears to exist between disordered states of the nervous system and diabetes. I think it may be put down as satisfactorily made out that instances have occurred in which diabetes has been directly produced by both injury and disease of the brain. I am also of opinion that functionally disordered states of the nervous system may constitute a cause of diabetes; and, right or wrong, my conviction is, that upon several occasions I have been able to trace the complaint to mental anxiety, or over mental work. Certainly I may assert that these conditions tend to aggravate materially the morbid state when the disease already exists.

Some relation appears to exist between carbuncles and boils and diabetes. It is certain that diabetics are more liable than others to become the subjects of these affections, and also what is closely allied—phlegmonous and gangrenous inflammation; and such complications have been not unfrequently known to constitute the immediate cause of a fatal termination. The converse relation has been also asserted to exist: that is, it has been maintained that the above-mentioned affections may lead to the production of diabetes. From what is contained in an article entitled "Du diabète dans ses rapports avec la gangrène spontanée, etc.," by Ernest Fritz, in the 'Archives Générales de Médecine,' tome i, 1858, glycosuria it would seem does not form so frequent an accompaniment of carbuncles, boils, &c., as was affirmed by Prout. It is here mentioned that the urine of 52 patients, 8 of whom were affected with carbuncle, 15 with boils, 22 with erysipelas, and 7 with diffused phlegmon, was examined by Wagner without sugar being found upon either occasion. Wagner, however, had twice seen glycosuria occur during the progress of carbuncle of a severe form.

According to Dr. Prout a diabetic condition is apt to occur in connection with gout and dyspepsia. In his work 'On Stomach and Renal Diseases,' fifth edition, p. 32, he says:—"Indeed a saccharine condition of the urine exists in dyspeptic and gouty individuals much oftener than is supposed; and hundreds pass many years of their lives with this symptom more or less constantly present, who are quite unaware of it, till the quantity of urine becomes increased."

I have often thought that I could trace a connection between diabetes and an irritable state of the alimentary mucous membrane. There is often to be observed a peculiar condition of the tongue,—a fissured condition for instance, and a morbidly clean and red or injected state of its surface, such that denotes irritation of the passage below. In many cases, also, much irregularity is observed in respect of the action of the bowels, diarrhœa and constipation alternating each other, and giving rise to a considerable amount of trouble. The idea, in fact, has occurred to me whether a certain state of the digestive canal may not, by reflex action through the sympathetic system, occasion diabetes.

Whatever the immediate exciting cause, it is quite certain that a susceptibility to diabetes is inheritable. My experience enables me to set forth many examples in which the disease was associated with a family predisposition.

A gentleman, for instance, aged sixty-eight, living at Huddersfield, whom I occasionally see, is the subject of diabetes. He belongs to a family of seven, and three in this family, besides himself, viz., two sisters and a brother, have been affected with the complaint.

A gentleman, about twenty-three years of age, who came to me in the last stage of diabetes, and died a few weeks afterwards, informed me that both his father and an aunt had died of the disease.

A former solicitor to the Treasury succumbed to the complaint a year or two ago. I learn from one of his relatives, my neighbour, Dr. Reynolds, that a daughter by the first wife died at twenty-two of diabetes, he himself at that time not being affected with the disease. A few years afterwards, however, he became so whilst exposed to much anxiety and mental hard work, viz., whilst engaged, on the prosecution side, in conducting the notorious Palmer trial. A daughter by his second wife is now the subject of diabetes at the age of twenty-one.

A patient whom I saw in February last, a gentleman, sixty years of age, informed me that he had been suffering from diabetes for a period of four years, and that nine years back a son had died, after a short illness, at the age of twenty-three, of the disease.

A clergyman, aged thirty, has been under my care nearly a couple of years. He tells me that an elder brother has also been affected with the complaint.

A medical man wrote to me, in October last, for my advice upon a case. His patient was passing, he stated, from two to three gallons of urine a day, presenting a sp. gr. of 1045 and loaded with sugar. In his note he mentioned that two of this patient's brothers had died of diabetes.

A lad, aged thirteen, from Lincolnshire, was under my care in Guy's Hospital for a short time in the spring of 1864. In May, 1865, I received a letter from his father stating that he had died in the autumn following, and that he feared a daughter, nine years old, had just become afflicted also with the disease. I desired that some urine should be sent to me for examination, and discovered that the fear expressed was well founded.

The son, a youth at school, of a medical man whom I had met in consultation at Tunbridge upon the case of another patient was taken with a most severe form of diabetes, which carried him off in the space of a few weeks. Shortly afterwards the father died of another complaint, and within a year the mother, who had never before manifested any symptom of diabetes, wrote to me saying that she had begun to suffer in the same sort of way as her son had done, and that she had thus been led to fancy that she was affected with the same complaint. Although thinking it not unlikely that her supposition would turn out to be the result of a groundless alarm, I desired her to come up to town in order that I might ascertain the truth; and upon investigation I found that diabetes in reality existed.

SYMPTOMATOLOGY.

Amongst the symptoms of diabetes that which, on the score of importance, claims attention first is an excessive flow of urine. It is by this symptom that the patient's attention is generally first aroused to the existence of something wrong. He finds that he is not only called upon to be frequently micturating during the day, passing a considerable quantity at each time, but that he is obliged to rise, it may be, several times during the night for the purpose of emptying the bladder. The actual quantity passed varies much in different cases, and according to the nature and success of the treatment adopted. It is not uncommon where the disease exists in a severe form and the patient is allowed to eat and drink what he chooses, for from ten or twelve to fifteen or twenty pints to be passed in the twenty-four hours. Instances have been recorded, however, where much larger quantities than this have been voided, and one has fallen under my observation where double the amount named was passed. The patient first came under my notice in the out-patient department at Guy's Hospital, and according to his account, he had ascertained by measurement that he was passing *twenty quarts* of urine a day. To ascertain if such a prodigious quantity really was being passed, I took him into the hospital and gave instructions that he should be supplied as nearly as possible with what he had been eating and drinking outside. His urine was collected and measured, and although the quantity did not quite come up to what he stated he had before been passing, yet it amounted upon one occasion to as much as sixteen quarts or thirty-two pints for the twenty-four hours, and upon other days also, before he was subjected to treatment, did not fall very far short of this.

In an uncomplicated case of diabetes, the quantity of urine may be taken as affording a very good rough index of the state of severity of the disease; and a diminution of it forms the first sign of improvement perceived by the patient under recourse to the appropriate measures of treatment. It is found that the patient has not to rise so many times in the night, and also that there is a less frequent call to pass urine during the day. In many cases the disease can, in the course of a short time, be controlled in such a way that the urine falls in quantity to about what is natural. Patients who may have been previously passing many pints in the twenty-four hours, may find the quantity sink to two or three pints and even less. I have at the present time a patient in the hospital who, upon admission, was voiding five pints in the twenty-four hours and now rarely passes above two—sometimes, indeed, only a pint and a half, and it has been upon two or three occasions as low as a pint and a quarter. Astonishment is not unfrequently excited at the rapid fall that is sometimes produced by treatment.

It must be acknowledged that it sometimes happens that the quantity cannot be reduced below five and six pints a day, and when such is the case it generally augurs badly for the future.

I have said that the quantity of urine may be taken as affording an index of the state of severity of the disease. It is found to fluctuate indeed, as a rule, very closely with the quantity of sugar escaping. The sugar in escaping may be said to entail an escape of liquid to carry it off, and thus the larger the quantity of sugar reaching the circulation for elimination the larger, *cæteris paribus*, will be the amount of fluid likewise carried off. I do not mean to assert that there is invariably a strict correspondence between quantity of sugar and quantity of urine discharged, for the latter is open to the influence of other circumstances besides the passage of sugar, but that the two, generally speaking, present a very close conformity is strikingly exemplified by the report of North's case to be found at the end of the volume—a case in which much fluctuation was induced by the different articles of diet that were administered. Upon giving attention to the report, it may be observed that with each rise and fall in the amount of sugar there was, excepting on but a few occasions, a corresponding variation in the amount of urine. If a line were introduced into the plan framed from the daily record of the case and introduced opposite page 238 to represent the daily amount of urine in drachms, it would be found to pursue a course throughout the greatest portion of its extent harmonising with the one which represents the daily amount of sugar. There is only one point, indeed, at which the lines would be found to cross each other, and this is under February 15th, upon which day the diet consisted of jelly, meat, and beef-tea. There was upon that day a considerable descent in the amount of sugar without, from some cause or other, a corresponding fall in the amount of urine.

Whilst speaking of an excessive flow of urine as a symptom of diabetes, the altered characters which the secretion presents may also be referred to.

The presence of sugar gives to the urine an increased density. Now, the quantity of sugar passed varies much in different cases and at different periods in a particular case, according to the circumstances existing. I have met with as much as forty-eight grains of sugar to the fluid ounce, but beyond about this, the quantity is never exceeded, the amount of urine being increased instead of a higher saturation occurring.

Where the degree of saturation with sugar is high, the density cannot fail to be at a high point also, but the converse does not happen invariably to hold good; a high density, in other words, may exist without being necessarily dependent upon the presence of a correspondingly large amount of sugar. This is owing to the weight of diabetic urine being influenced by the natural solids of the secretion as well as sugar. It may happen, from the circumstances of the case, that the urine is highly saturated with these, and thus a high sp. gr. will at once be given. This is not to be unlooked for under treatment by restriction to an animal diet. From the less quantity of sugar thereby discharged, the urine is diminished in quantity, and the large amount of animal food consumed gives rise to an extensive elimination of the ordinary solid urinary products. In this manner the sp. gr. may be maintained at a high point without there being any sugar passed. I have before me the notes of a case in which a medical man, himself the subject of diabetes, felt anxious about his state because the sp. gr. of his urine kept at a high point. A specimen that he brought me for examination showed a sp. gr. of 1035, but contained no sugar. The quantity passed was small, and being loaded with solid matter it threw down a copious deposit of lithates.

The density is sometimes regarded as though it supplied a knowledge of the amount of sugar contained in the urine. Taking the quantity of urine passed and the sp. gr. together, a rough estimate, it is true, can be formed of the extent of saturation with sugar, but the sp. gr. cannot be relied upon for indicating more. Instances are constantly occurring, in the experience of those who are in the habit both of taking the sp. gr. and estimating by analysis the amount of sugar, where a want of harmony exists in different specimens between the two. A striking example of such may be selected from the details of North's case, the report of which, as already mentioned, is furnished at the end of this work. On February 8th the urine passed between 1 and 5 a.m. presented a sp. gr. of 1032 and contained 23·05 grains of sugar to the fluid ounce, whilst that collected during a subsequent four hours, viz., from 9 a.m. to 1 p.m. was of a sp. gr. 1023, or nine degrees less, and contained 24·40 grains—rather more sugar, that is—to the ounce. Here, then, the sp. gr. and proportion of sugar actually moved in a converse direction to each other, and examples of the kind are not of unfrequent occurrence.

The sp. gr. of diabetic urine may reach as high as 1050, or, it may be, a little higher, but the usual range is from 1030 or 1035 to 1045. Where the disease has been controlled by treatment it may sink below the standard for healthy urine. Thus the urine passed by North between 9 a.m. and 1 p.m. on Feburary 15th, only presented a sp. gr. of 1010, and frequently during the progress of his case the sp. gr. was within a few degrees of this point.

The colour of the urine varies with the quantity that is passed. The disease does not influence the amount of colouring matter to be eliminated, and hence, when the quantity of liquid is greatly beyond what is normal it may present very nearly the appearance of spring water. By checking the amount of fluid discharged, the colour immediately more or less closely approaches that belonging to the healthy secretion. It will be found, if the urine passed at different periods of the twenty-four hours be collected separately, that the colour presents a marked variation. The urine passed on rising in the morning is, as a rule, much more highly coloured than what is passed at any other time, because from the non-ingestion of food during the night there is less sugar to be eliminated and the amount of fluid discharged is lessened accordingly. For the converse reason the urine passed upon going to bed at night is usually found to be about the palest of any. When a mixed diet is being taken the contrast in colour between the night and morning specimens is very great, but under the influence of an animal regimen there may not be much difference perceptible, the whole of the urine passed presenting, more or less, the colour of healthy urine.

Freedom from turbidity forms another of the characters usually belonging to diabetic urine. When the disease exists in a severe form the urine always remains bright and clear on cooling—never, in other words, throws down any lithate deposit, as is frequently observed to occur with ordinary urine. When successfully brought under control, however, a copious deposit of lithates may be found to take place. The patient sometimes takes alarm at the appearance which the urine thus presents; but he may be told that it is one of the best signs that can be witnessed. It indicates that the urine is no longer excessive in quantity. From the large amount of animal food consumed as a part of the treatment adopted there is a copious elimination of lithates. As long as the quantity of urine discharged is in excess, they are kept out of view by being held in solution, but directly the urine falls to about what is natural a precipitation ensues as cooling takes place, because the amount of liquid is now insufficient to keep them dissolved. The deposition occurring as the urine cools, and not before, is accounted for by the influence exerted by temperature upon the solvent power of the urine.

Under similar circumstances crystals of lithic acid also frequently show themselves, especially after the urine has been passed for some time. Healthy urine becomes alkaline on keeping, but with urine containing sugar the natural acidity may be increased through the occurrence of the lactic acid fermentation, and in this way the production of crystals of lithic acid will be promoted, just as happens upon the addition of an acid to a specimen of healthy urine.

Diabetic urine presents a peculiar odour which has been differently described by different authorities. It is to me an acid smell, and I think is due to the occurrence of the lactic acid fermentation. It is not unlike the smell perceived where ripe apples are kept.

It was formerly stated that urea was absent from the urine of diabetes, and the idea was entertained that the sugar partly appeared in its stead. From more recent investigations, however, this statement is negatived, and it even appears that a larger quantity of urea may be excreted during the existence of diabetes than under a state of health. This it may be considered is not in opposition with what might be expected, looking at the large quantity of food, and especially animal food, that is usually consumed by patients suffering from the disease, and taking into account the known physiological fact that one source of urea is the nitrogenized food introduced in excess of the requirements of the system. There is nothing, indeed, to show that any relation whatever exists between sugar and urea in the urine.

Albumen is sometimes found to accompany sugar in diabetic urine, and in examining urine it is always desirable to apply the tests for both.

In some cases the presence of albumen is evidently due to the existence of organic disease of the kidneys, just as in an ordinary case of Bright's disease, which in reality exists superadded to the diabetes. Under such circumstances the case naturally assumes much more gravity than as though it consisted simply of diabetes.

In other cases, however, only a small or moderate quantity of albumen may be present, and it need not necessarily betoken anything serious. I have known a slight quantity of albumen exist in the urine of diabetics for years without undergoing any increase and without apparently being of any import. It can be shown by experiment that the albumen of the food requires to be assimilated or converted into blood-albumen to obviate its escape with the urine. If the albumen of the white of egg, for instance, be introduced directly into the circulatory system—be allowed, in other words, to reach the general circulation without previously being acted upon by the digestive and assimilative organs—it immediately passes off with the urine. Now, it is possible that in the cases under review the appearance of albumen may be due to a defective assimilation in respect of this element, just as glycosuria may be dependent upon a faulty assimilation of sugar.

It is an interesting fact in connection with the passage of albumen and sugar together, that this has been sometimes observed to result from puncture of the medulla oblongata for the artificial production of diabetes. As mentioned under the head of pathology, from Bernard's investigations it appears that there is a particular spot in which the puncture is followed by glycosuria, another by polyuria, and another it may be by albuminuria. Now, it has sometimes happened that both glycosuria and albuminuria have been known to occur together after the puncture. In an experiment of my own, performed many years ago, the medulla oblongata of a dog was punctured for the purpose of producing artificial diabetes, and both albumen and sugar were afterwards discoverable in the urine. It is true, I could not positively say that the urine was free from albumen before the performance of the experiment, because it did not happen to have been tested for this principle, but there is every reason to believe that it was so, as the animal appeared in a perfectly healthy condition.

Before finishing what I have to say about the urine, I may refer to the effect of the presence of sugar in causing white spots to be left on articles of clothing where drops of urine have fallen. I have, before now, been able from this circumstance to trace back the commencement of the complaint, in the more chronic cases, to a period a considerable time anterior to its existence having been discovered. A patient, for instance, upon being questioned has recollected that for some time past he has noticed that his boots and the legs of his trousers have frequently become in a troublesome manner spotted over with white marks from the splashing of his urine from micturating upon the ground or against a wall. Trousers that have been put by, it may be for some time, have come out covered with a lot of white spots, occasioned by the drying of the sugar contained in the drops of urine that have happened to settle upon them. For the time that such has been noticed, it may be concluded that the person has been labouring under diabetes.

Next to an excessive discharge of urine, thirst may be considered as forming the most prominent symptom of diabetes. The thirst that is experienced when the disease is existing in a severe form is urgently complained of by the patient. It is a kind of thirst that cannot be quenched, however much fluid is taken. Patients have sometimes told me that they have been quite ashamed at the amount of fluid that they have felt obliged to drink. Not only the water-bottle, but the ewer on the wash-stand, has been emptied of its contents during the night, and more would have been drunk if it had been at hand. Before the nature of the complaint is discovered lemonade, beer, ginger-beer, and such-like prejudicial fluids, are consumed in large quantities, the effect of which is to aggravate the thirst. The patient does not know why, but the more he drinks the more he finds he wants to drink.

The unquenchable thirst of which diabetics complain is to be readily accounted for upon physiological principles. The sugar in escaping from the system carries with it water from the blood, and thus leaves this fluid in a more highly concentrated condition. Now, the solid and liquid matter of the blood ought to bear a certain relation to each other. To maintain this relation we have the action of the eliminative organs on the one hand, and a certain sensation on the other, which not only makes us conscious when fluid is required, but excites us with a strong desire to take it. No matter in what way the solid matter of the blood becomes out of proportion to the liquid—whether by the rapid loss of fluid from the cutaneous surface as by free perspiration—whether by the ingestion of a quantity of saline matter as from eating salt provisions—or whether from deprivation by a proper supply of drink—in each case the result is the same, a sensation is excited that we denominate thirst, which has the effect of inducing us to take what is wanted to restore the balance that has been disturbed. Thus, thirst is designed for securing that the blood is maintained with a due proportion of fluid; and such is the strength of the sensation when fluid is urgently needed, that an irresistible desire to drink is excited. By the thirst which accompanies diabetes a replacement of the fluid that is being so extensively discharged by the kidneys is induced in accordance with what is naturally required.

The symptom of thirst may be taken as affording, in an ordinary case, an index of the state of severity of the disease. The greater the quantity of sugar reaching the circulation, the greater will be the amount of fluid passing off by the kidneys, and the greater the sensation of thirst excited.

An excessive appetite is also a frequent accompaniment of diabetes. The sense of hunger arises from the requirement of solid matter in the system, just as thirst arises from that of fluid. Now, seeing that so large a proportion of what is consumed fails to be applied to the purposes of life, and escapes from the system under the form of sugar, it is not surprising that this symptom should be encountered. In a severe state of the disease the appetite is something truly enormous. The patient finds it difficult to appease his hunger, and unless food be frequently taken great discomfort is experienced. What I am speaking of applies to the disease whilst allowed to exist in an uncontrolled form. Under appropriate treatment this excessive appetite very soon diminishes, and in the course of a short time the desire for food is brought within ordinary bounds. It is desirable that the patient should be made aware of this to encourage him in adhering to the restricted diet, which at first he may complain of as not being bulky enough to give him a sense of satisfaction.

There is a peculiar sensation, not exactly hunger, referred to the stomach, which the diabetic is generally well acquainted with. It is described as a feeling as though a hollow or empty space existed at the pit of the stomach which nothing seems to fill up. It is always much mitigated, if not entirely removed, as the case improves under treatment. I have met with a few cases in which there has been something quite remarkable about this sensation of hollowness or emptiness. In one, particularly, the patient was impressed by it that she was sinking, and was led, in consequence, to exclaim every now and then to those around her that she felt that that particular moment must be her last.

The state of the mouth is often much complained of by the subjects of diabetes. A dryness is experienced which fluids fail to have the power of alleviating, and the tongue cleaves in a uncomfortable manner to the palate. The lips are also parched, and frequently a slight accumulation of dried mucus is apt to be visible about the angles of the mouth. To those accustomed to be thrown much in contact with diabetics, the state of the mouth alone will sometimes suffice to lead to the suspicion of the existence of the disease. The patient as he is speaking is constantly rolling the tongue, in a peculiar manner, about in the mouth, and passing it over the lips, apparently with the view of distributing what moisture he can over the surface; and from sticking as it does to the palate, on account of the dryness that exists, a sound is produced which is very significant and suggestive to those who have once given attention to it.

The tongue varies considerably in appearance in different cases. Sometimes there is nothing special to be observed. Sometimes, however, it is morbidly clean and intensely red, and perhaps also fissured. In this state it presents very much the aspect of raw meat. Sometimes it is covered with a white creamy fur, whilst at other times the fur is dry and brown.

Diabetics sometimes experience, as a subjective sensation, a sweet taste in the mouth. It disappears as the disease is subdued by treatment, and may be perceived again directly anything is taken which sends up the sugar in the urine. I have heard this sensation before now spoken of as affording a sign by which the patient could tell if he had been taking anything injurious to his complaint.

As to the cause of this perception of sweetness, it may be suggested whether it depends, as the saliva does not happen to constitute a secretion that is impregnated with sugar, upon the circulation of saccharine blood through the gustatory papillæ. In support of this notion it is stated to have been found by Magendie, that on injecting bitter solutions into the veins of dogs the animals afterwards manifested the same signs of perceiving something disagreeable in the mouth as when the solution was introduced directly into the mouth itself; and that on injecting, instead of the bitter solution, a relishable liquid, such as beef-tea, the animal licked its mouth as though an agreeable impression were perceived; of course the suggestion here would be, that the materials which had been introduced into the blood influenced the extremities of the gustatory nerves whilst passing through the vessels of the papillæ, just as they would do on reaching them through the mucous membrane in the usual way.

The teeth are not unfrequently observed to become loosened in diabetes, and it may be even to such an extent as easily to drop out. There is evidently some direct connection between this phenomenon and the disease. It seems as if the morbid condition of the system prevailing interfered with the nutritive action going on in the fang and its socket, and so led to the result. It is only when the symptoms are allowed to run on in a severe form that it is noticed, and supposing the teeth to have become already loosened, I have known them again become firm upon the disease being controlled by treatment.

Few diabetics have anything to complain of in respect of digestive power. It seems as a rule to be even stronger than in ordinary people. Although an enormous quantity of food is sometimes consumed, no sense of weight at the stomach or other symptom of indigestion is experienced. One patient, that not long ago fell under my observation, informed me that he had been a martyr to dyspepsia until he became the subject of diabetes, but that since then he had not known what it was to experience anything of his old complaint.

It must not be understood, however, from what has been said, that the digestive power is invariably good, or continues invariably good throughout. Sometimes there is such a loss of appetite and even loathing of food, that the patient can be induced to take but little. Sickness also sometimes prevails, and may constitute a symptom of importance.

Constipation is a very common accompaniment of diabetes. From the extensive loss of fluid taking place through the kidneys, the system is left with a deficient amount, and as one of the results the contents of the large intestine become so unnaturally dry and hard as to render their expulsion difficult. Rules, however, are not without their exceptions, and it happens in this case that the opposite condition to constipation may be found to prevail. Diarrhœa sometimes comes on without apparent cause, and may prove very difficult to check. With some of the diabetic patients that have died in Guy's Hospital, and whose cases I have there come across, the prostration produced by profuse diarrhœa has appeared to constitute the immediate cause of death. Altogether, the state of the bowels usually forms a source of great discomfort to the diabetic, and very difficult to manage properly. It may happen that as constipation is overcome diarrhœa sets in, and then again the reverse, the patient thus being harassed with one inconvenience or the other.

The skin is usually complained of as dry and harsh. The sound produced as the patient rubs his hands together affords evidence of the dryness—the parchment-like character of the skin—that exists. On looking at the palms, the cuticle is not only observed to be unnaturally hard and stiff, but the lines or furrows corresponding to the seat of flexion present a white and mealy instead of a transparent appearance. As the disease becomes subdued this unnatural condition of the skin disappears. The patient is thus furnished with another criterion which enables him to judge of the condition he is in.

As regards perspiration the ordinary account given is that the patient has not known what it has been to perspire since his disease has set in. Strangely enough, however, looking at the evidence of the deficiency of fluid existing in the system, sometimes even with the disease at its height, the patient will be found to perspire at times profusely. One case I remember which particularly attracted my attention in consequence of this phenomenon. The patient was an inmate of Guy's Hospital, and suffering from a severe form of diabetes unattended with any pulmonary complication. On my visit to the ward I often found him lying on his bed bathed in perspiration, drops of which stood thickly upon his face.

In speaking of the state of the skin it should here be mentioned that a rash, especially lichen, is sometimes observed as a concomitant of diabetes. I have seen cases in which acute lichen has shown itself and produced very serious disturbance. In females it is not uncommon for the external genitals to become the seat of extensive swelling and irritation. This condition seems to be produced by the direct irritating effect of the urine, and most severe inconvenience or even distress may for a time be occasioned in this way. Also, but much less frequently, in the neighbourhood of the orifice of the male urethra there may be a kind of excoriation observable.

There is a peculiar odour eliminated from the body of the diabetic. It is strongly perceptible in the breath when the patient is desired to breathe under the nose of the observer. Many persons, especially ladies, can recognise something peculiar in the atmosphere of a room in which a diabetic has been sitting. My own sense of smell is not sufficiently acute for the purpose, but I have known instances where a person without any previous knowledge of the fact has exclaimed on entering a room, and exclaimed correctly, that a diabetic has been in it. The odour eliminated has been differently described by different authorities. According to my own experience it more resembles the smell of ripe apples than anything else. It is the same kind of smell, in a milder degree, that is evolved from the urine. Dr. Prout speaks of it as a sweetish hay-like odour.

The general appearance which the diabetic presents in a well-marked case is often to an experienced eye quite sufficient to lead to a pretty safe presumption that the disease exists. Simply from this it not unfrequently happens that the physician is able to pick out the diabetic from amongst a number of patients. It is difficult to describe exactly what it is that enables him to do so, but when the appearance has once been seen it is easily recognised whenever it is come across. Emaciation forms one of the conditions observed. Besides this there is a peculiar care-worn pinched-up appearance of the face. The features are drawn, and the expression dejected, and indicative of the bodily distress which accompanies the disease.

As regards this bodily distress the patient does not complain of any actual pain. He cannot localize his suffering to any particular part, neither can he describe exactly what he feels. There is, indeed, a general feeling of indescribable uneasiness, distress, or discomfort throughout the body which renders him despondent and miserable. From this indefinite description of uneasiness a clue is sometimes given that may lead to the recognition of the disease.

The emaciated and sunken appearance which the face presents in diabetes is doubtless in great part due to the deficiency of fluid contained in the tissues. It is astonishing what an amount of difference a few days may make in the appearance of the face in each way, either under a sudden and marked aggravation of the symptoms on the one hand, or an amelioration on the other. A few days' accession of urgent symptoms may suffice to give the patient a totally altered appearance for the worst. The improvement, also, that is sometimes produced by a few days' treatment is looked upon by the friends as truly marvellous. The main cause of this rapid alteration is evidently due to the change which occurs in the amount of fluid contained in the tissues.

A real waste of tissue, however, rapidly goes on when the disease exists in a severe form. The patient's flesh vanishes, and his loss of weight in a very short time may be extreme. As the case yields to treatment, not only is the loss that has been taking place stayed, but a gain begins to show itself, and under favorable circumstances the patient may find before very long that he is about as heavy as he was before the disease set in. The weight, it may be remarked, is usually studiously watched by the patient, and more relied upon as an index of his progress than anything else.

It is not to be wondered at that the tissues should be drawn upon and wasted, seeing that so large a portion of the food escapes being turned to account as it ought to be. Further proof than we possess is not needed to show that starch and sugar become converted into and constitute one source of fat in the animal system. Deprive an animal of the power of elaborating or assimilating these principles, and this source of fat—and it may be regarded as forming an important one in the mixed and vegetable feeder—is immediately cut off. Now, in diabetes there is a want of assimilative power over these elements, and thus they fail to contribute, as they should do, to fat production.

Debility of a greater extent is complained of than what can be accounted for simply by the emaciation that is noticed. The presence of the sugar that exists in the blood must be regarded, I think, as rendering it unsuited for properly contributing towards muscular action, muscles being dependent for their power of contraction, not only upon a due vascular supply, but upon a proper state of the blood. North, when subjected to the varied dieting mentioned in the report of his case, complained directly he was put upon a diet that caused him to pass an extensive quantity of sugar that he seemed to have no life, energy, or muscular power about him. The rapid change perceived can only be satisfactorily accounted for by looking upon the blood when highly charged with sugar as ceasing to hold a healthy relation to the tissues. The most marked example of muscular debility that I remember to have seen occurred in an hospital patient who had just come over from America. He was so weak when he applied for admission that he had to be supported into the hospital by a couple of friends, and could not stand alone. Under the change that took place as the result of treatment, in about three weeks' time, proud of his strength, he ran to the end of the ward and back again to show what he could do.

What has been said in respect of muscular action will apply also in explanation of the loss of virility which accompanies the inveterate form of the disease. The condition which the blood presents may be considered as unsuited for the maintenance of functional activity in the organs in question. In support of this view it may be stated that as the disease is subdued and the blood restored to a natural condition virility is found to return. Referring to North's case again, loss of virility was recounted in his history as having existed since the commencement of his illness. A few days after he had been placed upon an animal diet and the morbid condition thereby reduced, he confidentially mentioned to the clinical reporter that he felt sure he must be getting better, on account of a particular circumstance that he had noticed. He had hitherto, he said, been like a child since he had been affected with the complaint, but now he found that "his nature" had returned.

In the female subject a suspension of the catamenia may be looked for whilst the symptoms of the disease are severe, and its restoration when they become controlled.

In addition to what has been mentioned about the muscular system, it may be stated that cramp forms a frequent accompaniment of diabetes. Some patients complain urgently of cramp in the legs, which seizes them night after night, and gives rise to much inconvenience. If the discharge of sugar can be controlled by treatment, a disappearance of this symptom along with the others of diabetes may be confidently looked for. In cases, however, where only a partial mitigation of the disease can be effected, although cramp may not have been present as an early symptom, it is not unlikely to be experienced as the case runs on.

Œdema of the legs must be enumerated as one of the occasional concomitants encountered. According to my experience it is but rarely observed, but I have known instances in which it has existed for a time to a marked extent, and has given rise to much alarm in the mind of the patient. I am not aware, however, that it need be looked upon as bearing any particular import; at all events, I have seen it disappear as the disease has been controlled, the case ultimately turning out satisfactorily. Of course I am referring here to œdema accompanying diabetes uncomplicated with kidney disease. Bright's disease is sometimes associated with diabetes, and may give rise, as when existing alone, to dropsy. In such a case a grave opinion only can be formed as regards the future.

I have alluded under the head of pathology to the special liability that exists to the occurrence of boils, carbuncles, and gangrene in association with diabetes. Carbuncles and gangrene sometimes constitute the immediate cause of a fatal issue. As long as the disease can be kept under control the patient may be regarded as occupying a safe position, but during the passage of highly saccharine urine the state of the system is such that a very slight disturbing cause may suffice to give rise to the most serious consequences.

It should be borne in mind that such a simple measure as the application of a blister during the existence of the diabetic state has before now been followed by the development of a carbuncle which has led to the death of the patient. Dr. Gull some time ago mentioned to me an instance of this kind which fell under his own observation. The friends of a medical practitioner who formed the subject under consideration were warned against resorting to the employment of a blister, as had been proposed, for symptoms of cerebral disease, on account of the co-existence of a saccharine state of the urine. A blister was, nevertheless, subsequently applied to the nape of the neck; and soon, a large carbuncle became developed, which led to the production of a fatal result.

The susceptibility to the occurrence of these affections is probably due to a low state of vitality in the tissues, produced by the unnatural condition of the blood that exists. The same is also probably the explanation of the liability that is noticeable to the supervention of pulmonary disease. If the complaint is allowed to run on in an unchecked state, I think it may be said that the most likely unfavorable event to happen is the supervention of pulmonary disease, which may ultimately constitute the immediate cause of death.

The chronic form of pulmonary disease so frequently encountered in association with diabetes is commonly spoken of as phthisis; but although it runs the same course and presents the same symptoms as tubercular phthisis, yet it seems in reality to constitute a result of simple chronic inflammatory action, attended with breaking down of the lung tissue and the formation of cavities without being preceded by or accompanied with any strumous or tubercular deposit. I have alluded to this form of disease under the head of pathology, and unless the grey induration that is met with around the cavities, which many consider as the product of common inflammatory action, be looked upon as of a tubercular nature, there is no tubercle belonging to the affection. What I am referring to constitutes the pneumonic phthisis of Dr. Addison, and this I contend forms the kind of pulmonary disease that is commonly encountered in connection with diabetes; but, of course, I do not deny that cases may happen in which true tubercle, as in other cases without diabetes, may be found.

I regard, then, the phthisis or chronic disease of the lungs specially accompanying diabetes as a chronic inflammatory action, dependent on the presence of such an amount of sugar in the blood as to alter its natural quality, and to render it unfit for the healthy discharge of its functions. It will be admitted that the blood requires to possess a certain composition to enable it to administer, in a proper manner, to the healthy performance of nutrition and the other functions of life; and it is generally agreed upon in physiology that the actions taking place under the existence of a natural relationship between blood and tissues lead to the development of a force which materially contributes towards aiding the circulation. By a disturbance of this relationship, as must occur with the existence of an unnatural state of the blood, a weakening of this force may be expected to ensue; and thus, an influence—an influence say arising from exposure to cold, that would not affect a healthy person, may lead in the diabetic to the production of a local congestion, that may be followed by inflammatory action. It is in this way, I believe, that the frequent association of disease of the lungs with diabetes is to be accounted for; and in support of this view it may be stated that it is only when the diabetic complaint is allowed to run on in an uncontrolled state that a special proneness exists to the development of pulmonary disease. My experience enables me confidently to say that but little fear need be apprehended when the sugar is kept down by treatment of pulmonary disease becoming developed. Should the case, under these circumstances, proceed to an unfavorable termination, it will be almost sure to be in some other way.

As well as the chronic form of lung disease that has been spoken of, acute pneumonia is of frequent occurrence in association with diabetes. A large proportion of the deaths that appear amongst the mortality returns of Guy's Hospital with diabetes recorded against them have pneumonia also mentioned. In these instances the patient, as a rule, has been admitted with the double disease upon him, and so serious is the complication that there exists but little chance of recovery.

Sometimes cases occur in which there seems to be a sudden stasis of the pulmonary circulation. In illustration of this I may mention the case of a young woman who was sent up to me for admission into the hospital from the country. There had been no particular urgency observable in her symptoms previously, but she apparently took cold on the journey, and within an hour or two after admission was seized with intense dyspnœa and died in less than twenty-four hours. A *post-mortem* examination was made, and universal engorgement of the lungs without anything further was discovered.

The following particulars of an analogous case were supplied to me by Dr. Gull. A gentleman, whose urine was found to be strongly saccharine, was first of all suddenly seized with swelling of the right leg, attended with evidence of an obstructed circulation through the limb. Recovery from this took place, but confirmed diabetes existed. From exposure to cold a year afterwards an attack of sudden passive congestion of the lungs without any signs of pyrexia set in and carried the patient off within forty-eight hours.

Instances of this kind tend to show upon what a delicate balance the circulation in these cases hangs. Dr. Prout very appositely speaks of the frail tenure of life held by diabetics. He mentions cases to show how they exist, as it were, on the brink of a precipice; the fatigue and excitement of a long journey to consult him having proved, he states, sufficient to give rise to fatal consequences in four instances within the space of a few years. In taking this statement into account it must be remembered that a long journey in former days meant something very different from what it means at the present time. In cases where the discharge of sugar can be and is kept down by treatment the patient may be regarded as occupying as safe a position as an ordinary person; but, where the reverse holds good, he is liable at any time, from the operation of a slight disturbing influence, to the supervention of mischief of the most serious kind.

The blood of diabetics has been regarded as presenting a peculiarity in respect of physical appearance. In the article on "Blood," by Dr. B. Guy Babington, in Todd's 'Cyclopædia of Anatomy and Physiology,' a milkiness of the serum is spoken of as existing and constituting something peculiar.

My attention has been given to this point, in the opportunities that have occurred to me, of examining diabetic blood removed by bleeding and cupping. In two instances I have observed this milky character very strongly marked; whilst in others the serum has only been slightly lactescent or not lactescent at all.

I am not disposed to think, however, that there is anything special about this milkiness of the serum in diabetes, because I have frequently noticed in my physiological experiments, and the same has been noticed by others upon the human subject, that when blood has been removed a few hours after the ingestion of food, especially food rich in fatty matter, the serum has been strongly lactescent, and on being allowed to repose has given rise to an accumulation of a thickish cream-like layer upon the surface. This cream-like layer on being examined microscopically has presented the appearance of the molecular base of chyle, and doubtless, therefore, has been directly derived from the chyle. During fasting there is no such appearance to be observed. Now, diabetics usually consume a large quantity of food, and particularly of food likely to lead to a plentiful introduction of fat into the system. The milkiness of their blood, therefore, may be quite unconnected with any peculiarity belonging to their disease, but simply dependent on the flow of fatty matter into the blood through the chyle in accordance with what takes place under natural circumstances.

Where the abstraction of blood is resorted to in acute febrile and inflammatory complaints the circumstances of the case would scarcely, if ever, allow us to expect that a milkiness of the serum would be likely to be found. Now, such being the complaints for which the removal of blood is most generally performed, we are afforded an explanation of why the character of milkiness is not of more common observation than it is.

I do not know whether it has any bearing worthy of consideration towards connecting the liver with the complaint, but I may remark that I have noticed the serum of diabetic blood present a height of yellow tinge that I have not observed under ordinary circumstances.

I have alluded to disease of the lungs as frequently constituting the immediate cause of an unfavorable termination in diabetes. Coma is also another common occurrence through which death is ushered in. I believe where the disease has been partially kept under control, that this may be regarded as forming the ordinary way in which death takes place, should death occur from the complaint. The result of my experience as regards termination amounts indeed to this: where the disease is allowed to run on in a severe and uncontrolled form the chances are that pulmonary mischief will become developed and carry the patient off; where the disease, on the other hand, has been partially controlled, if an unfavorable issue should ensue, it will in all probability take place through the supervention of coma; lastly, where the disease has been completely or almost completely controlled, the measure of control being formed by the state of the urine, no danger need be apprehended as long as this fluid is observed to exist in a satisfactory condition.

I cannot explain the cause of this coma, but it closely resembles the coma which sometimes occurs in association with albuminuria. Indeed, medical practitioners in writing to me about cases where this mode of termination has happened have before now described their patient as having sunk under uræmic poisoning. As a rule it is preceded by great weakness and prostration, a quick and feeble pulse, and often irritability of the stomach, which may amount only to nausea or may lead to actual vomiting. Then the intellect becomes blunted, and soon coma gradually sets in and becomes more and more profound without any return of consciousness until death supervenes, it may be in the course of a few hours, or the patient may linger on in this state for two or three days. Sometimes the coma may come on more rapidly, the patient becoming excessively weak or faint, and soon exhibiting signs of unconsciousness, which go on increasing until it is complete, but it cannot be said that it comes on suddenly under the form of a fit, as is not of uncommon occurrence in cases of albuminuria. The condition appears as though it resulted from the effects of blood poisoning, and looking upon it in this light the term "glycohæmia" might be made use of upon like grounds that "uræmia" is employed to comprehend the analogous train of phenomena sometimes occurring in connection with Bright's disease.

Before I quit this part of my subject there is one more point that I must refer to, viz. the occurrence of cataract in association with diabetes. This has somewhat recently excited a considerable amount of interest and attention on account of its having been lately discovered by experiments conducted upon the lower animals, that cataract may be induced artificially by the introduction of sugar into the system.

Dr. Prout, in the fifth edition of his work on 'Stomach and Renal Diseases,' 1848, p. 32, referred under the form of a note to the association of diabetes with cataract:—"As other instances," he says, "of diabetic derangement and debility I may state that I have seen two cases of the disease accompanied by cataract. The one in a gentleman between fifty and sixty (lately dead); the other in a young man between twenty and thirty. The young man had been successfully operated on, and when I last saw him appeared likely to recover his sight."

No particular attention seems to have been afterwards given to this matter until Mr. France ('Ophthalmic Hospital Reports,' January, 1859, and 'Guy's Hospital Reports,' 1860 and 1861) placed upon record an array of cases strongly tending to show the existence of some immediate connection between the occurrence of cataract and the presence of diabetes. One of Mr. France's cases was originally admitted into Guy's Hospital under my own care, in July, 1860, and remained under my charge for a short time previous to being transferred to the ophthalmic department under Mr. France. The case was that of a woman aged thirty-four, who at the time of admission was passing from four to six quarts of urine, with a sp. gr. of 1040, a day. Her impairment of vision had gradually come on, and both eyes were affected alike. From Mr. France's examination it was found that there existed symmetrical, opalescent, lenticular cataracts with superficial striæ of unusual bulk. She could find her way about the ward without assistance, and could distinguish large objects before her, but could not see sufficiently to discern their outline. Her diabetic complaint had been of about two years' duration, and about five months had elapsed since she commenced to notice her sight failing.

It is to Dr. S. Weir Mitchell that we are indebted for proving experimentally that a connection exists between cataract and a saccharine state of the system.

The results of his experiments were made known in an article entitled "On the production of Cataract in Frogs by the administration of Sugar," published* in the 'American Journal of Medical Science' for January, 1860. It seems that whilst performing some experiments upon the osmosis of woorara through animal membranes Dr. Mitchell accidentally found that the injection of a certain amount of syrup beneath the skin of frogs occasioned death within a few hours; and, at the same time, produced a white appearance of the eyes, which proved to depend upon cataract. The following is an extract from the account given of one of Dr. Mitchell's experiments:

"*Experiment.*—About two drachms of syrup were injected under the skin of a large frog. In twenty-four hours the lens was opaque, and as the animal appeared lively it was placed in water in order to test the permanence of the opacity. Ten hours in the water sufficed to remove most of the opacity from the lens, which began to clear in the centre first. Twenty-four hours after the frog had been placed in water the eyes were perfectly transparent and the animal itself entirely well."

Dr. Mitchell also observed that the same effect could be produced by soaking the eyes of frogs, or the lenses themselves, in a solution of sugar; and, when cataract had been established, that it disappeared on placing the lenses in water. The conclusions he sums up with are:—"*First.* That sugar in large amounts destroys the life of the frog when given internally, injected under the skin, or thrown into the stomach. *Second.* That an abundant supply of water frequently enables the frog to eliminate the sugar and escape death. *Third.* That the formation of a peculiar variety of cataract is one of the most curious and striking symptoms attendant upon the sugar poisoning. *Fourth.* That the cataract is due to mechanical disturbances of the form and relative position and contents of the component tubes of the lens."

Dr. Richardson ("The Synthesis of Cataract."—'Journal de la Physiologie, par E. Brown-Séquard,' 1860) has repeated Dr. Mitchell's experiments and obtained confirmatory results. He has also tried the effect of a great variety of other solutions, and has found them to act in the same way as syrup, with the exception of the iodide of potassium, which left the lens unaffected in every case. In the summary he has given he says—"In the first place it is to be observed that the success of the experiment in producing the cataractous condition turns on the specific gravity of the fluid injected. It required in every example that the specific gravity should exceed 1045, in other words that it should exceed the specific gravity of the blood. But so soon as a condition of the blood was obtained, so soon as the circulating fluid could afford secretions, having an abnormal density, then the cataractous change was induced, and lasted so long as the blood retained its abnormal state."

These experiments, therefore, in a conclusive manner confirm the inference that had been drawn from clinical observation, viz. that a direct connection exists between the occurrence of cataract and the existence of diabetes. I have seen in the course of my experience several cases where the association has existed. I wish to mention, however, that I have not unfrequently met with defective vision in association with diabetes where no cataract has existed to account for it. In some of these cases the impairment has appeared to depend upon a want of the proper amount of adjusting or accommodating power of the eye through weakness, or paresis of the ciliary muscle.* I have come across cases which may be put down as cases of this kind; and, in these, to the astonishment of the patient, the application of Calabar bean to the eye has been followed by a marked improvement of sight in the space of half an hour, objects which before had been but indistinctly seen at a short distance from the eye having become distinctly visible.

* Mr. Bader, in his work on 'The Natural and Morbid Changes of the Human Eye,' makes the following remark in speaking of cataract in diabetic persons:—"Choroidal or retinal complications are rare, while paretic or paralytic affections of the ciliary muscle are frequent."

TREATMENT.

The object to be attained in the treatment of diabetes is to control the elimination of sugar, and according to the extent that this can be effected the symptoms of the disease are subdued. There are two plans of treatment which, as a rule, require to be put into practice together. In the first place, we aim at correcting by medicinal agents the morbid disposition which prevails; and, in the next place, have to avoid feeding, as it were, the disease, by excluding from the diet those principles which fail to be properly disposed of in the system. Cases, it is true, are sometimes met with in which the disease can be controlled by medical treatment alone, but in general nothing effective can be done without the assistance also of restriction to a particular scheme of diet. These two plans of treatment — medicinal and dietetic — will be considered separately, and it will be convenient first of all to speak of the latter.

The opinion expressed by Dr. Prout, that "the first and chief point to be attended to in the treatment of diabetes is diet," is fully endorsed by the experience of the present day. With a healthy person, when saccharine and farinaceous materials are ingested, as in partaking of bread and many other vegetable articles of food, they are lost sight of in the system, because there exists an aptitude for assimilation whereby they are rendered available for administering towards the requirements of life. Their physiological destination fulfilled, their elements, it may be fairly presumed, escape chiefly in the form of carbonic acid and water from the body. With the diabetic, however, such kind of food, instead of being appropriated, is allowed to pass through the system unemployed. A morsel of bread being eaten, the starch is converted into sugar, but the transformation proceeds no further. There exists an incapacity for carrying on the process of assimilation, and, as the consequence, the sugar formed reaches the circulation and thence the kidneys, by which organs it is discharged unchanged, its passage through the system producing the symptoms of derangement which belong to the disease.

The object, it will be readily conceded, to be kept in view in the treatment of diabetes is to place the system of the patient in a state as closely approaching the healthy standard as possible. In no complaint have we, I believe, so clear an indication of what is to be done as in this. In diabetes, in particular, the management of the case is open to rational principle for our guidance. An element of food, from a want of capacity for properly disposing of it, makes its appearance in the circulation and gives to its contents an unnatural condition. If we take into consideration the enormous quantity of sugar which may be voided by a diabetic, evidence is presented of the extensive deviation from the healthy state in the condition of the blood that may prevail. In the case, for instance, of a patient who was found upon one occasion to pass under a mixed diet twenty-one pints of urine containing 47·05 grains of sugar to the fluid ounce in the twenty-four hours, rather more than 19,000 grains, or upwards of 2¾ lbs. of sugar, traversed the circulation during that period, and must necessarily have given to its contents a highly unnatural condition. Now, to reduce this deviation from the healthy condition in the state of the blood to the minimum degree that can be attained forms what is to be specially aimed at in treatment. The desirability of placing the contents of the circulatory system in as physiological a state as possible will scarcely be disputed, in order that they may be in a position for healthily administering to the functional operations of life.

To abstain from the particular element of food, which fails in the diabetic to be assimilated, forms the rational course to adopt to assist in accomplishing the object that has been referred to. Fortunately the withdrawal of this alimentary principle from the food does not in itself entail any injurious consequences. There are those, indeed dwelling in some parts of the globe who habitually subsist without it. Its place can be supplied by another principle, viz. fat, which fulfils the same physiological purpose, but connected with which there is no defective power of appropriation apparent in diabetes.

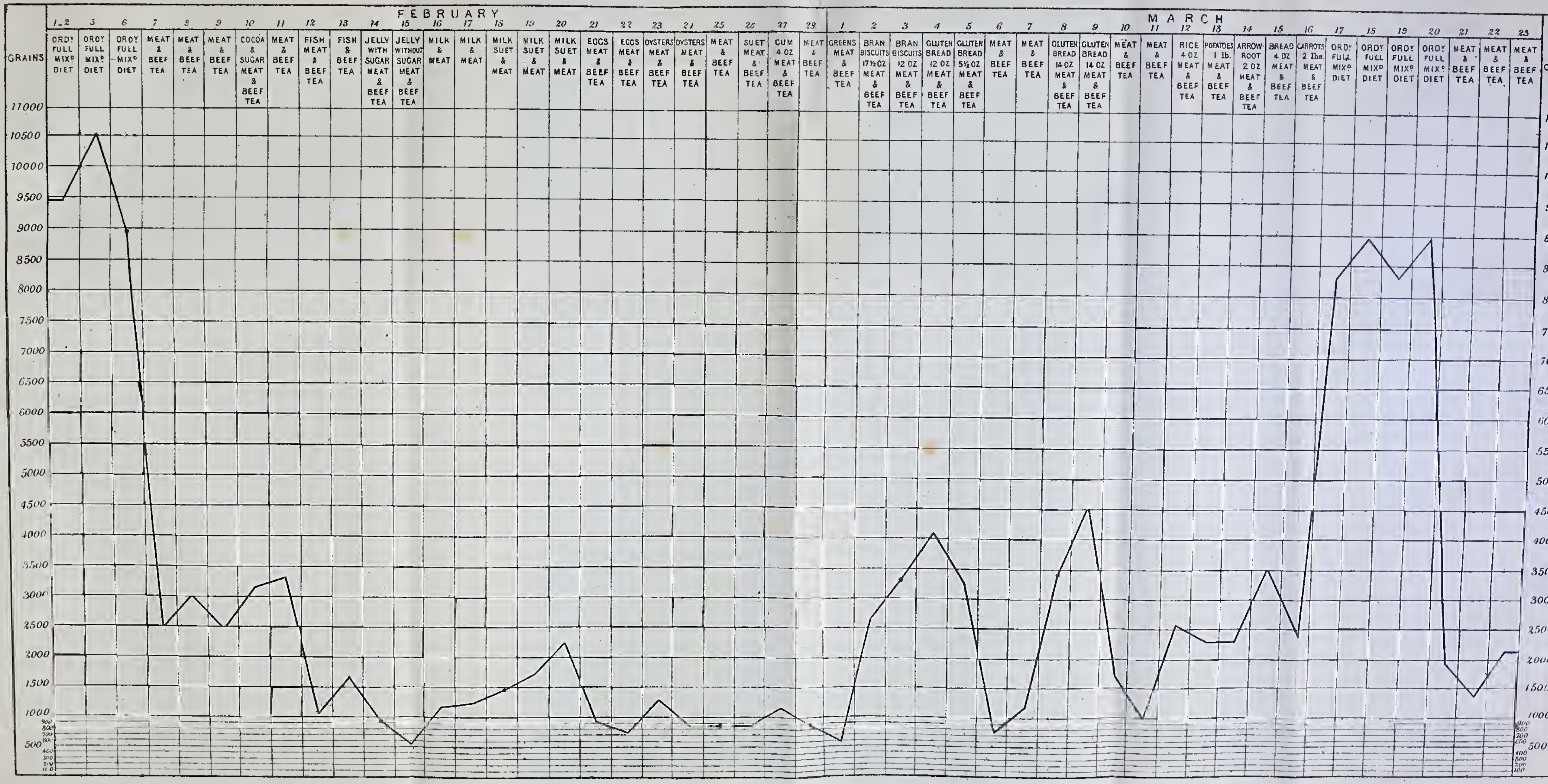
Restriction from saccharine and farinaceous articles of food, in some cases, temporarily removes every sign of the complaint. I have already referred to cases of this description. Bouchardat as far back as 1841 noticed the phenomenon, and placed on record, in the 'Comptes Rendus de l'Académie des Sciences,' two cases illustrative of the fact.

In the ordinary form of the complaint, although the restriction in diet subdues the symptoms, yet the sugar may not entirely disappear from the urine. Notwithstanding this, however, its reduction in amount, I feel most strongly, places the patient in a position not only of much greater comfort but likewise of much greater security than he otherwise would be. A diabetic who is passing a large quantity of sugar and continues upon an unrestricted diet enjoys but a very insecure hold upon life. Under the abnormal state produced by a saturation of the system with sugar very slight causes are sufficient to set up disturbances which may prove of the most serious import to the patient. External influences which might lead only to a trivial and temporary derangement in a healthy person may give rise, in an uncontrolled case of diabetes, to the production even of a fatal result. From what I have seen I am strongly of opinion that when by dietetic measures the elimination of sugar is kept down, the patient is not in the same way liable to those incidental complications which so frequently produce a fatal termination in diabetes allowed to run on in a severe form. I do not go so far as to say that diabetes may always be prevented from proving fatal, for it would seem that a form of disease may occur in which there is something else to deal with besides the mere functional aberration connected with the assimilation of sugar. It must be admitted, in fact, that cases are met with in which there exists a source of interference with nutrition beyond what can be accounted for by the mere presence of sugar in the blood; for although the discharge of sugar may be kept down below what is noticed in other cases where no material disturbance is perceptible, yet the disease may be found to make progress in weakening and emaciating the patient until ultimately an unfavorable termination is produced. It would seem in these cases as if the cause which determines the saccharine state of the blood does also something more than this, and affects deeply the nutritive processes of the system. Should such, in reality, prove to be the case, the error in respect of sugar would form only one phase or manifestation of the complaint.

The influence producible by diet upon the elimination of sugar in diabetes has for some time past been known; but to ascertain for myself the effect of different articles of food in the disease, I some time ago submitted a case to careful observation in Guy's Hospital. The patient voluntarily assisted in the investigation that was conducted, and faithfully, I am convinced, carried out the instructions that were given to him. For a period of nearly two months he was subjected to different kinds of dieting. The urine secreted for every four hours was collected separately. Six specimens, therefore, were procured, for every twenty-four hours and these, after being measured, were all from day to day carefully examined by myself. The case is placed by itself at the end of the book, and I confidently advance the report as a truthful record throughout; for, not only was the patient kept under strict supervision, but scrupulous care was in every way taken to secure the utmost precision that was possible.

From the results obtained the accompanying plan has been constructed, which shows at a glance the effect produced by different articles of food upon the amount of sugar eliminated by the patient. I have thought it advantageous to introduce the plan here instead of placing

PLAN SHEWING THE VARIATION IN THE DAILY AMOUNT OF SUGAR PASSED UNDER DIFFERENT DIETS BY JOSEPH NORTH, ÆT. 32, A DIABETIC.



it with the report. From the position of the fluctuating line upon it the number of grains of sugar passed per diem can be read off by means of the scale inserted on either side, and above can be seen the nature of the diet consumed. For information regarding the quantity of food where this is not mentioned I must refer the reader to the details of the report.

The rapidity with which the effect of food manifests itself upon the urine, is shown upon several occasions in the case. On February 10th, for instance, after a purely animal diet had been adhered to for a few days, the patient deviated from his instructions, and took with his tea at 4 p.m. some prepared cocoa sweetened with sugar, which his friends, during the afternoon, had brought him in. During the four hours between 1 and 5 p.m., the quantity of sugar voided was 468 grains. During the succeeding four hours the quantity rose to 1311 grains, and the next four hours descended again to 483 grains. On March 12th, again, after having been for a couple of days on a purely animal diet, he was ordered some rice. At 6 a.m. he ate for breakfast half a rice pudding composed of 4 oz. of rice and 1 egg. From 1 to 5 a.m. the quantity of sugar passed was 81 grains; whilst from 5 to 9 a.m. it amounted to 576 grains. On the following day he took for breakfast at 6 a.m. 1 lb. of potatoes without anything else. From 1 to 5 a.m. the sugar eliminated was 281 grains, and from 5 to 9 a.m. 794 grains.

The above examples suffice to show how rapidly the ingestion of sugar-yielding substances produces an influence upon the urine. Some time ago, however, Mr. G. N. Bacon undertook some further observations for me upon this point, and I will here introduce the results he obtained. The case submitted to observation was that of a lad seventeen years of age, an inmate of the Norfolk and Norwich Hospital under the care of Dr. Ranking.

In one series of observations the urine secreted four hours before, and four hours after breakfast was collected and examined, the patient being allowed wheaten bread *ad libitum*, milk, tea, and sugar.

		Quantity of urine.	Quantity of sugar.	Proportion of sugar to fluid-ounce.
		oz.	grains.	grains.
Jan. 6th.	4 hours before breakfast	22	575	26·
	4 hours after breakfast	28	1344	48·
„ 7th.	4 hours before breakfast	18	432	24·
	4 hours after breakfast	21	1008	48·
„ 13th.	4 hours before breakfast	12	345	28·8
	4 hours after breakfast	23	1104	48·

In another series the patient was supplied with gluten instead of wheaten bread, and milk and tea, but no sugar. Here it will be noticed the difference in the amount of sugar passed before and after the meal was not so marked, on account of the smaller quantity of saccharine and farinaceous principles ingested.

		Quantity of urine.	Quantity of sugar.	Proportion of sugar to fluid-ounce.
		oz.	grains.	grains.
Dec. 30th.	4 hours before breakfast	26	439	16·92
	4 hours after breakfast	20	720	36·
Jan. 1st.	4 hours before breakfast	22	288	24·
	4 hours after breakfast	20	822	41·10
„ 2nd.	4 hours before breakfast	16	384	24·
	4 hours after breakfast	24	986	41·10

Upon another occasion the urine secreted, four hours before, and four hours after dinner, consisting of meat, gluten bread, watercress, and brandy and water, was collected and examined. It must be taken into consideration on looking at these results that the urine before the meal was under the influence of the previous one which he had had the same day.

		Quantity of urine.	Quantity of sugar.	Proportion of sugar to fluid-ounce.
		oz.	grains	grains.
Dec. 14th.	4 hours before dinner	20	639	31·98
	4 hours after dinner	24	864	36·
„ 15th.	4 hours before dinner	16	576	36·
	4 hours after dinner	26	936	36·
„ 17th.	4 hours before dinner	20	822	41·10
	4 hours after dinner	24	767	31·98

The information supplied by the case given at p. 180 goes to show that, not only may the starch and sugar ingested traverse the system unappropriated, but, that their ingestion may act in such a way upon the complaint as to give rise to the elimination of more sugar than could be derived from the principles themselves. Thus, after sugar had for some days been entirely absent from the urine under restriction to an animal regimen, two ounces of ordinary bread per diem were, for a couple of days, allowed, and then the restricted diet again resumed. During the first day that the bread was taken the patient passed 117 grs. of sugar, and during the second 196 grs. The following day he passed 213 grs.; the next, 571 grs.; then, 236 grs.; and lastly, 92 grs. After this there was an absence of sugar. By the four ounces of bread, therefore, the elimination of 1425 grs. of sugar was occasioned, which is more than could be derived from the bread itself; for I found that two ounces, after being perfectly dried in a water oven, left a residue weighing 600 grs. The whole of the solid matter in the bread consumed consequently only amounted to 1200 grs., against the 1425 grs. of sugar discharged with the urine. Another point worthy attention is, that the elimination of sugar continued increasing for two days after the bread had been discontinued, and that it was not until after the sixth day from the commencement of its being taken that the urine regained a non-saccharine character.

The exclusion of saccharine and farinaceous materials from the diet has now been generally acknowledged for some years past as forming one of the essential points, to be attended to in the treatment of diabetes. This, to be strictly carried out, involves an abstinence from almost all the ordinary kinds of vegetable food. Although there can be little doubt, looking to the form of our teeth, the character of the articulation of the lower jaw, and the general inclination of mankind, that we are designed by nature to subsist upon a mixed diet, yet our capacity for adapting ourselves to varied external circumstances is such as to admit of restriction to either an animal or vegetable diet without any harm arising.

A vegetable diet, for instance, forms that upon which some of the native tribes of India subsist, and there are many, even amongst Europeans at home, who restrict themselves to vegetable food and do not find that their vegetarian mode of life leads to anything wrong.

There are those, again, on the other hand, who subsist entirely on animal food, and physiologically an animal regimen contains all that is requisite for the support of life in a healthy manner. The Arctic Highlander is obliged to restrict himself to an animal diet, because he can procure no other. It wisely happens that an animal diet, richer in fat than a vegetable as it is, is the best suited to the circumstances under which he is placed; but independently of this, the character of his climate altogether precludes the growth of those vegetable products which enter into the mixed diet of the inhabitants of other regions. According to the account of an exploration of Baffin's Bay given by a northern voyager, the most conspicuous vegetable productions of the Arctic Highlands consist of heath, moss, and various coarse grasses. There was no appearance, it is stated, of cultivation, nor was it discovered that the natives made use of vegetable food.

Besides those who practise restriction to an animal diet through necessity, others adopt it from some other cause. Upon this point, Dr. Carpenter, in his work on the 'Principles of Human Physiology,' says:—"There are particular conditions of existence, however, under which life may be advantageously supported upon *animal* food alone. Thus the Guachos of South America, who pass the whole day in the saddle, and lead a life of constant activity resembling that of a carnivorous animal, scarcely ever taste anything but beef; and of this their consumption is by no means great; for the temperature of the surrounding atmosphere is so high, that the body has no occasion to generate more heat than is supplied by the combustion of the hydro-carbonaceous portion of the 'waste' of the tissues." Among the trappers and hunters of North America it is also stated to be a common thing for a man to be months without tasting bread or any thing of the kind.

In carrying out the exclusion of starch and sugar from the diet, it is not necessary that complete restriction to animal food should be enforced. There are some vegetable substances that may be allowed, and sufficient to admit of a fair amount of variation at the meals. The greatest privation encountered is in respect of bread and as a substitute for this there are three kinds of food—the gluten, bran, and almond—specially prepared for the diabetic. Upon each of these I shall have some remarks to offer.

The manufacture of gluten bread was first undertaken at the instigation of Bouchardat, of Paris. The 'Comptes Rendus de l'Académie des Sciences' for November, 1841, contains a communication, entitled "Nouvelles recherches sur le diabète sucré ou glycosurie,' in which he suggests the use of gluten bread in diabetes, and gives cases to show the advantage of its employment. This article of food at once met with a favorable reception, and soon became widely known. It is prepared in Toulouse and Paris, and imported into this country in the form of slices and rolls. It may be procured in London at Van Abbot's Dietetic Depôt, 5, Princes Street, Cavendish Square. Being perfectly dry it keeps very well, and by placing it over steam it may be moistened and rendered soft, like recently made bread. It also admits of being toasted. The rolls I have found are liked better than the slices. Gluten flour is also to be obtained of Mr. Van Abbot, and may be applied to a variety of culinary purposes in the place of ordinary flour.

The chief complaint that is made by patients against the gluten bread is, that as they eat it it seems as though they were chewing india-rubber. Another objection is, that it is not suited, certainly to be consumed in quantity, in severe cases, on account of its not being sufficiently free from starch. In the preparation of the gluten from flour, it is true a large proportion of the starch is washed away, but still a considerable quantity is left behind. A drop or two of a solution of iodine allowed to fall upon the bread shows by the almost black colour that is produced, that a large quantity of starch is present. North's case also, as may be seen upon referring to the plan, shows that it exerts a decided influence upon the urine. It was given upon two separate occasions, and each time the sugar rose to a somewhat considerable height. It must be stated, however, that a larger quantity of the food was consumed than would ordinarily be wanted. The gluten, if carefully prepared, might be rendered much more free from starch than that of which the bread is found to be composed, but to remove all the starch would constitute a troublesome process, and it seems further that the gluten is thereby deprived of the properties which give it its virtue as a bread-forming agent.

Mr. Bonthron, of 106, Regent Street, has recently succeeded in producing some gluten biscuits and bread, which are more eatable than anything of the kind I have yet met with. The biscuits present somewhat the character of a cracknel. They eat short and crisp, and are readily reducible in the mouth; have no unpleasant taste; and, consumed with other food, possess the power of cleansing the palate. The bread is moist, and will not keep good for more than about ten days. Its consumption, therefore, involves a frequent supply. It serves to increase the variety at the command of tho diabetic; and, independently of this, possesses the advantage of presenting an approach to the condition of ordinary bread.

Next, as regards the preparation of a substitute for bread from bran. Dr. Prout ('On Stomach and Renal Diseases,' fifth edition, p. 44) says:—"For some time past I have recommended as a substitute for bread in diabetes, a compound of bran, eggs, and milk, which, if properly prepared, is not unpalatable." He further states that a patient to whom this bran bread had been recommended took much pains to perfect the process of preparation, and then describes what had been found to be the best method of procedure to adopt. The late Dr. Camplin, who had been for many years a diabetic, and had effectually succeeded in keeping his disease at bay, spoke very strongly, from personal experience, in favour of the bran food as a substitute for bread in diabetes, and suggested a great improvement in its mode of manufacture. Dr. Prout simply directed that the bran should be washed to remove adhering starch, and therefore used it in a very coarse state. Dr. Camplin directed his attention towards getting it reduced to a minutely divided condition, and so placing it in a much more suitable form for employment. He found that after being well washed, and then dried, it could be reduced, in a mill specially contrived for the purpose, to a powder of a degree of fineness almost equal to flour.

Mr. Blatchley, of 362, Oxford Street, worked under Dr. Camplin's instructions and prepares the bran according to his recommendation. He has for many years devoted himself to preparing the bran food, and manufactures a biscuit which has had an extensive sale. It is made as palatable as the nature of bran will allow, and what is of vast importance may be relied upon, according to my experience, as having been prepared in a careful way. Unless the bran has been well washed previous to being employed it will be contaminated with a quantity of starch, and will thence fail to represent what is wanted. It is therefore essential that the bran should be prepared with care to avoid frustrating the end in view. Some time since a patient who had been hitherto progressing in the most satisfactory manner, came to me complaining of a return of his symptoms. He assured me that he had made no alteration in his mode of living. I examined his urine and found that he was passing a large quantity of sugar, much more than I could understand should be the case under the circumstances, as far as they were known to me. I felt convinced that there must be some deviation somewhere, but the patient was quite unconscious of where it could be. At last, after having gone minutely into detail and without making any advance, the patient incidentally produced from his pocket a specimen of the bran biscuits he had lately been consuming, and which he said instead of being procured, as at first, of Mr. Blatchley, had been made for him by a baker in the provincial town where he resided. The difficulty was now at once cleared up. A simple inspection sufficed to show that they contained a quantity of flour—in fact, consisted almost of meal. I need scarcely say that I at once condemned them as unfit for his use, and upon returning to the old biscuits, his symptoms, as I had anticipated, quickly became subdued. A baker who is not acquainted with the necessity of securing as strict an exclusion of starch as possible, will, even, not impossibly, without meaning to do anything wrong, put in a little flour, with the view of pleasing his customer by making the biscuits as palatable as he can.

It is no uncommon grievance with the diabetic to have loose and bad teeth, and the hardness of the ordinary bran biscuits renders them difficult to eat. To meet this emergency Mr. Blatchley supplies a softer kind of biscuit which he distinguishes by the name of bran-cake.

By means of the bran flour a very fair article of food may be made in the patient's house, and I am constantly recommending this plan to be adopted, at the same time giving to the patient a recipe, which was handed to me by a lady, the wife of a diabetic, who had contributed much to her husband's comfort by devising various palatable substances for his use. Believing this recipe will be found of service, I will introduce it in the form of a note below.* When the directions are properly carried out a substitute for

* *Recipe for bran cakes.*—Take 4 oz. of prepared bran flour, 2 oz. of butter, 1 drachm of bicarbonate of soda, 5 eggs, and about a quarter of a pint of warm milk. First mix the bicarbonate of soda with the bran flour. Then beat up 2 oz. of butter in a hot basin and shake into it the mixture of bran flour and bicarbonate of soda, beating with a spoon all the while. Next beat up the 5 eggs in a separate basin before the fire till milk warm and stir them gradually into the mixture of bran flour, soda, and butter. Beat up all well together for at least ten minutes, adding gradually the warm milk. Place in well-buttered tins or patty-pans, and bake in a brisk oven for about ten minutes. The cakes are done when they will turn out of the tins quite easily. The above quantities will make about five cakes of the size of ordinary buns. The cakes, if desired, may be cut into slices, toasted, and buttered.

Instead of all bran flour, equal parts or other proportions of bran and almond flour may be used. The cakes, in the opinion of many, are thus rendered more palatable. The almond flour seems to soften and neutralize the taste of the bran; whilst the bran reduces the richness of the almond flour.

bread is yielded, which may of course be supplied to the patient fresh every day or as often as may be desired, and which is really not unpalatable. It ought to be light, soft, and moist, without giving an impression of feeling wet or cold in the mouth.

After the process to which the bran is subjected in washing it may be questioned if it possesses really any nutritive value; but as it is employed it is combined with other materials, and it plays the part of an unobjectionable agent which gives bulk to what is consumed, and therefore supplies something for filling the stomach and enabling the patient to feel that he has taken a full meal. It must be said that the bran flour is not altogether free from starch, but it is much freer from it than the gluten, and observation shows that the amount of sugar passed under its employment is less than under the employment of gluten. In a severe case where it is desired to exclude as strictly as possible saccharine and farinaceous materials from the diet, the bran food is to be selected in preference to the gluten.

A specimen of bran flour prepared by Chapman and Co., St. James' Mills, Hatcham, has been recently sent to me for inspection. I am informed it has been subjected to a thorough washing with hot water—a process which from what has been already said is indispensable, and it appears to have been very fairly deprived of starch. I have had a portion of it made into cakes, and find that its fineness renders it susceptible of being readily disposed of in the mouth. It also possesses very little taste.

The state of the alimentary canal varies in different diabetics, and in some the irritability is such that the bran food gives rise to diarrhœa and cannot on this account be continued with. Usually, however, a tendency to constipation prevails, and the use of an indigestible and slightly irritant material like bran produces a beneficial effect in stimulating the muscular fibres and secreting glands of the intestine into increased activity.

The almond food originated with myself. Looking at the drawbacks that existed with regard to the starchy grains I turned my attention to products of the vegetable kingdom from which starch is absent. The almond is of this kind and forms an edible and nourishing article. The hemp seed also pretty closely resembles the almond in chemical composition, and is to be purchased at considerably less cost, but there are difficulties in the way of separating the husk from the kernel which deprive it of equal adaptability for the purpose of food.

According to an analysis of Boullay, almonds contain 54 per cent. of oil, 24 per cent. of emulsin—a nitrogenized substance, 6 per cent. of sugar, 3 per cent. of gum and some woody fibre, &c. The oil may be considered as occupying the place of the starch in the cereal grains.

Dr. Pereira in his work 'On Food and Diet,' 1843, p. 340, says, "Sweet almonds are nutritive and emollient, but, on account of their fixed oil, difficult of digestion, at least when taken in large quantities or by persons whose digestive powers are weak." This remark general experience will confirm, and it equally applies to the hazel-nut, filbert, walnut, Brazil-nut, cocoa-nut, and, in fact, to all the oily seeds. The reason, however, of their difficult digestibility is easily explained, and the difficulty at the same time easily overcome.

In the process of digestion a solution of the food is effected by the agency of a watery fluid poured out by the stomach—the gastric juice. It is the nitrogenized alimentary principles that are dissolved by this fluid—oily matter remains to be acted upon by other secretions poured out further on. Now, for the gastric juice to be placed in a position for exercising its solvent influence, it must needs be in contact with the principle to be dissolved. The more intimately the gastric juice can be incorporated with the constituent particles of the food the more favorable, *cæteris paribus*, will the circumstances be for the accomplishment of digestion. Hence, the assistance afforded by mastication, the food being by this process reduced to a minutely divided state, so that an intimate incorporation with the gastric juice can take place when the stomach is reached. With a tough oily seed like the almond it is not likely that a thorough reduction of it will be effected in the mouth. Small unreduced or uncrushed pieces are swallowed, and these, from their impregnation with oil, will resist the penetration of the gastric juice. Thus the solvent action can only be carried on at the surface; and, as the result, the process of solution will constitute a lengthy or tardy process.

The difficult digestibility of the almond, in fact, arises from the disadvantageous position under which it is placed, by virtue of its physical state, for being acted upon by the solvent juice of the stomach. By being ground to a fine powder previous to being presented for consumption, the circumstances are altered, and it no longer offers the same resistance to the influence of the stomach, and it is in this form that it is employed as diabetic food.

The oily character of the almond renders it indeed a desirable article of food for the diabetic. There is a want of power in the disease to turn to account one form of heat-producing food, namely, the saccharine and farinaceous, whilst with the other, the oleaginous, there exists no difficulty. Theoretically, the diabetic should be supplied pretty largely with fat, and practically it is found that its effect is highly beneficial. Dr. Prout, in a note at p. 40 of his work on 'Stomach and Renal Diseases,' 5th edit., says, "We may observe here that oleaginous matters often agree so remarkably well in diabetes that some have gone so far as to propose them as remedies. When freely taken they usually cause a flow of saliva and thus diminish the urgent thirst. When they agree also, they give a sensation of satisfaction and support to the stomach which other alimentary substances do not." This last remark exactly coincides with an expression that was made use of by North after he had been partaking for three days pretty largely of suet. The expression made use of was that he liked the suet, and that it filled up the void which seemed to exist at the pit of his stomach more than anything else he had yet taken.

Theoretically and practically, then, it would seem that the almond, with its 54 per cent. of oil taking the place of the starch of the cerealia, is admirably adapted to supply the diabetic with a staple article of food. From the large amount of nitrogenised matter which the almond also contains—viz. 24 per cent., it forms, in addition, a material that must possess highly nutritive properties. It is not quite free from objectionable constituents; containing, as it appears to do, according to the analysis given, 6 per cent. of sugar and 3 per cent. of gum. The sugar exists under the form of cane sugar, and therefore to be susceptible of recognition by the copper test it must first be converted into grape-sugar, which is easily effected by boiling for a short time with a few drops of dilute sulphuric acid. No trace of starch is to be encountered in the almond.

The sugar and gum are easily extracted, and when this has been done an alimentary material is left as unexceptionable for the diabetic as animal food. In effecting the separation it is, of course, desirable that nothing else should be removed, as a loss would be thereby occasioned. The nitrogenous matter existing in the almond and comprehended under the term emulsin gives water the power of taking up and holding in suspension the oily matter present, thereby forming an emulsion, or, in fact, an almond milk. The nitrogenous matter of the almond holds, in fact, a position in this respect identical with that held by the caseine of animal milk. Now, in getting rid of the sugar and gum, by the agency of water, it is necessary to avoid the production of an emulsion. I find that the retention of the oily matter is to be thoroughly effected by keeping back or rendering insoluble the nitrogenous matter. Without the presence of this latter in solution, the oily matter fails to be taken up, or an emulsion to be formed. On taking the ordinary emulsion and boiling it, a considerable coagulum is formed; but still the liquid remains milky, although in a much less degree than before. Upon the subsequent addition of a small quantity of acid, another coagulum is formed, and now the liquid becomes clear. In fact, the almond contains both albumen and caseine, and in order to coagulate or render both insoluble, an acidulated boiling liquid must be used. Either, then, by treating almond powder with boiling water slightly acidulated with tartaric acid, or soaking the almonds in a boiling acidulated liquid which may form part of the process for blanching, the sugar may be removed without disturbing the oily or nitrogenous matter.

Mr. Blatchley, whom I have before referred to as supplying the bran biscuit, supplies also the almond biscuit in an elegant-looking and palatable form. By many diabetics it can be taken, and is considered a desirable accession to the other kinds of food allowed, but it must be admitted that by some it is found too rich for ordinary consumption with the meals. It goes very well, however, with a little sherry or any other kind of wine alone, and, composed as it is entirely of almond flour and .eggs, it forms a highly nutritive and serviceable food. It is eaten well by children, and I am of opinion might be found advantageous in other cases besides diabetes where a highly nourishing article is required.

In an hospital case where the almond biscuit was given and the amount of sugar passed determined, the following results were obtained:—For five days to start with the patient was allowed an ordinary mixed diet, and the amount of sugar ranged from 4500 to 6256 grains per diem. During the following nine days he was put upon an animal diet with greens. The amount of sugar varied between 864 and 1536 grains per diem. The next two days his diet consisted of animal food with 8 oz. of gluten bread. Upon the first day the sugar passed amounted to 1715 grains, and upon the second 1767 grains. Upon the following day the diet consisted of animal food with 4 oz. of gluten bread and 4 oz. of almond biscuit, and 1318 grains formed the quantity of sugar passed. The next day the diet consisted of animal food with 6 oz. of gluten bread and 2 oz. of almond biscuit. The sugar rose to 1618 grains. Next, for four days, the animal food was given with 8 oz. of almond biscuit and no gluten bread. The amount of sugar passed per diem stood as follows: 1219, 1346, 1233, and lastly 672 grains. A little later, under an animal diet with 8 oz. of gluten bread, the patient passed 2099 grains of sugar one day, 1825 grains the next, and 1703 grains the day after. Then for five days 8 oz. of almond biscuit were substituted for the gluten bread. Upon the first day 1305 grains formed the quantity of sugar passed; upon the second, 1375 grains; the third, 784 grains; the fourth, 1152 grains; and lastly upon the fifth, 1110 grains.

In another case, where the urine was specially examined for the purpose of obtaining a representation of the effect of the almond food, the following are the results that were yielded:

Date.	Quantity of urine.	Sp. gr.	Amount of sugar per fluid-ounce of urine.	Quantity of sugar per 24 hours.	Diet.
	oz.		grains.	grains.	
April 11	180	1040	40·	7200	Full mixed diet.
„ 12	190	1036	40·	7600	
„ 13	180	1036	37·50	6750	
„ 14	160	1041	40·	6400	
„ 15	220	1035	38·70	8514	
„ 16	230	1038	41·35	9510	
„ 17	190	1037	40·	7600	
„ 18	60	1042	38·70	2322	Animal diet, with greens and 8 oz. of almond food.
„ 19	80	1017	8·20	656	
„ 20	70	1019	9·	630	

A specimen of almond flour has been sent to me by Mr. Darby, of the firm of Darby and Gorden, of 140, Leadenhall Street, City, which forms a great improvement upon the almond powder I have before seen. It is in about as fine and nearly as white a state as ordinary wheaten flour. With the almond powder previously obtainable the large quantity of oil contained in it rendered it too rich for some persons to be able to take it. With this preparation a great portion of the oil has been removed by pressure, and thus a product is presented much more closely resembling, in its physical properties, ordinary flour. It may be used in a variety of ways that will at once suggest themselves to those who are at all experienced in the culinary art. It may take the place of flour as a thickening agent. Mixed with gluten it forms a kind of artificial flour which may be used just as ordinary flour would be employed. With cream and gelatine it furnishes a very good blanc-mange.

In carrying out the dietary scheme required for excluding the ingestion of starchy and saccharine principles, it happens, on account of the extensive diffusion of these through the vegetable kingdom, that not only must wheaten bread and such like food, whether derived from barley, oats, rye, maize, or rice, be prohibited, but likewise most of the vegetable alimentary substances in common use, as will be seen from what follows, must be abstained from.

The leguminous seeds, including peas, the garden or broad bean and the French bean or haricot, like the cerealia, contain a large amount of starch.

Macaroni, vermicelli, Italian paste and semolina are prepared from wheat, and, as may be shown by the tincture of iodine, abound in starch.

The farinaceous foods such as sago, tapioca, and arrowroot must, of course, be avoided.

The potato, according to the analyses mentioned in Pereira's work on 'Food and Diet,' contains starch varying in amount from 9·1 to 24·4 per cent.

Carrots, parsnips, beetroot, turnips, and onions contain sugar.

As regards other kinds of vegetables, it may be said that those vegetable products which have not been exposed to the sun's rays, and rendered green thereby, contain sugar. Hence, cauliflower, Brussels sprouts, broccoli, cabbage (I mean, the mature vegetable with white heart), seakale, celery, and asparagus, are, strictly speaking, more or less objectionable. As the result of exposure, during growth, to the influence of the sun's rays, it is found that not only is green colouring matter developed, but that the sugar which previously existed disappears. Thus, the green tops of asparagus are devoid of sugar, whilst the white part below is freely charged with it. Such is, also, what may be noticed with the green leaf and the white stalk of the celery plant. Indeed, anything in the way of leaf and leaf stalk that has been allowed to become green by exposure to light, may be considered, as far as sugar is concerned, as forming unobjectionable food in diabetes. Greens, therefore, of the different kinds, and spinach may be freely consumed.

It is only when the dietary requires to be carried out in a very strict manner that all the above-mentioned vegetables spoken of as containing sugar need be forbidden. Carrots, parsnips, and beetroot, like the farinaceous vegetables, such as peas, beans, and potatoes, in almost all cases, certainly at first, must be prohibited.

Turnips, Brussels sprouts, broccoli, and the rest may be often allowed, and especially after having been boiled in a large quantity of water, by which a considerable portion of the sugar they contain is removed.

What has been said above about colour with respect to vegetables will apply also to salads. Water-cress are quite free from sugar. Green lettuce may be taken *ad libitum*, but that which is white is not altogether free from objection. Radishes and celery contain some amount of sugar, but not enough to prohibit their use in moderation.

All fruits, on account of their saccharine nature, must be scrupulously avoided. For dessert, therefore, the diabetic has to fare but badly. The oily seeds, such as the hazel-nut, filbert, walnut, brazil-nut, sapucaia-nut, and almond may be taken, but it must be remembered that they are not perfectly devoid of sugar, although totally devoid of starch. The chestnut is a different product altogether; it abounds in starch, and therefore must be avoided.

Pickles and condiments may be employed to encourage the appetite and assist the patient in consuming his animal food.

Cream and butter may be used in making sauces, but no flour. The gluten flour, almond flour, or yolk of egg, however, may be employed as thickening agents instead.

Some have suggested that glycerine may be made use of as a sweetening principle. It does not belong to the carbo-hydrate group, its composition being $C_6H_8O_6$. It would not be expected, therefore, that it would lead to an increased elimination of sugar, and yet such, from observation, appears to be the case. To a patient who was being restricted to an animal diet, and who was passing from 3 to 3¾ pints of urine, and from 900 to a little over 1100 grains of sugar in the twenty-four hours, I ordered glycerine to be administered. Upon the first day he took six ounces, upon the second eight ounces, and upon the third ten ounces. The urine rose in quantity to between five and six pints, and the sugar to from upwards of 2000 to upwards of 3000 grains *per diem*. The glycerine being omitted, the urine immediately fell in quantity, and averaged for several days about three pints, and the sugar about 1500 grains. Glycerine was then given again to the extent of ten ounces a day for four days consecutively. The urine rose, and upon the third day reached eight pints; and the fourth day 7¾ pints in quantity. The sugar upon the first day amounted to 3744 grains; the second, 4032 grains; the third, 4608 grains; and the fourth, 4850 grains. The glycerine being now discontinued, the urine on the following day stood at three pints, and the sugar at 2540 grains. The next day the urine amounted only to 2¼ pints, and the sugar 1199 grains. The glycerine employed was that supplied to the Guy's Hospital dispensary. Whatever the explanation, the fact is indisputable, that under its use a material aggravation of the complaint was produced. With the increase in the quantity of urine and that of sugar, the patient experienced a return of thirst, and expressed himself as altogether feeling worse. The quantity of glycerine ordered was purposely large, and to get it taken it had to be administered at frequent periods throughout the day.

Attention requires to be paid to the fluids as well as the solids that are consumed. Milk is often recommended on the score of its forming an animal product. It must be taken into consideration, however, that amongst the constituents of milk there is a saccharine principle—lactin, which is present in cows' milk, according to the analyses given, to the extent of 3 or 4 to 6 per cent. It would be an unintelligible exception if the presence of lactin did not render milk an objectionable article of food in diabetes. That milk does in reality act prejudicially upon the urine may be seen by reference to the report of North's case. During the five days, February 16th—20th, that this patient was taking milk—three pints a day—the amount of sugar passed steadily increased from 1198 to 2225 grains for the twenty-four hours; and, on the following day, the milk having been taken off and two pints of beef tea allowed instead, fell to 927 grains.

Amongst stimulant beverages there are several wines that may be allowed. Claret, burgundy, chablis and hock, form wines that may be taken at discretion. Sherry varies considerably as regards the existence of sugar. Some specimens upon examination I have found to be perfectly devoid of sugar, whilst others have been charged with a considerable amount. The most likely to be free from sugar or to contain the least of this principle are the amontillado, manzanilla and vino de pasto. Dry sherries of other descriptions may be also met with pretty nearly free from sugar. A fruity sherry is objectionable. The sherry in use at Guy's Hospital which I examined some time ago yielded me upon analysis sixteen grains of sugar to the fluid ounce. Port wine contains sugar in largish quantity. A specimen of old port that I submitted to analysis was found to be charged to the extent of rather over seventeen grains to the fluid ounce. A specimen of Guy's Hospital port was found to contain thirty-seven and a half grains to the ounce.

Brandy and other unsweetened spirits are allowable to any extent that may be considered needful.

Sweet wines, sparkling wines, cider, perry, the ordinary old and mild ales, porter, and stout must be strictly forbidden. The Burton bitter ale, however, may be taken in moderation. A specimen of Bass's bottled bitter ale, procured from a retail establishment, only yielded an indication of containing just over two grains of sugar to the ounce. Specimens of draught bitter ale — Bass' and Allsopp's — contained rather more.

As regards non-stimulating beverages, either tea, coffee, or cocoa from the nibs, may be allowed. Soda-water generally proves exceedingly grateful, and may be taken as desired. Lemonade, on account of the sugar it contains, must be prohibited.

In commencing the restricted diet the patient may at first complain that he feels what he takes is not sufficiently bulky to thoroughly satisfy him. If he will only exercise a few days' perseverance, however, he will find that his appetite lessens and that he no longer experiences any inconvenience upon this score. Nothing so effectually relieves both the inordinate appetite and thirst as the exclusion of starch and sugar from the food.

It may be as well to remark for the sake of those who look to the sp. gr. of the urine as affording an indication of the progress of the case that allowance must be made for the density being naturally high under a large consumption of animal food. It is a well-known physiological fact that the ingestion of animal food notably influences the amount of solid matter eliminated with the urine. The specific gravity, therefore, may remain at a highish point notwithstanding a material reduction has taken place in the amount of sugar.

Founded upon the principle of excluding starch and sugar from the food the annexed dietary scheme has been framed in which most of the ordinary articles of consumption amongst us are referred to.

DIETARY FOR THE DIABETIC.

MAY EAT

Butcher's meat of all kinds, except liver.
Ham, bacon, or other smoked, salted, dried, or cured meats.
Poultry.
Game.
Fish of all kinds, fresh, salted, and cured.
Animal soups not thickened, beef-tea, and broths.
The almond, bran, or gluten substitute for ordinary bread.
Eggs dressed in any way.
Cheese. Cream cheese.
Butter. Cream.
Greens. Spinach.
Water-cress. Mustard and cress. Lettuce.
Celery and radishes sparingly.
Jelly, flavoured, but not sweetened.
Blanc-mange made with cream, and not milk.
Custard made without sugar.
Nuts of any description, except chestnuts.

MUST AVOID EATING

Sugar in any form.
Bread, wheaten or otherwise.
Rice. Arrowroot. Sago. Tapioca. Macaroni. Vermicelli.
Potatoes. Carrots. Parsnips. Turnips.
Peas. French beans.
Cabbage. Brussels sprouts.
Cauliflower. Broccoli.
Asparagus. Seakale.
Pastry and puddings of all kinds.
Fruit of all kinds, fresh and preserved.

MAY DRINK

Tea. Coffee. Cocoa from nibs.
Dry sherry. Claret. Burgundy. Chablis. Hock.
Brandy, and spirits that have not been sweetened.
Soda-water.
Burton bitter ale, in moderation.

MUST AVOID DRINKING

Milk, except sparingly.
Sweet ales, mild and old. Porter and stout. Cider.
All sweet wines. Sparkling wines. Port wine, unless sparingly.
Liqueurs.

Before I pass to the consideration of the medical treatment of diabetes I may refer to two plans of treating the disease, which appear to have originated with M. Piorry, of Paris, and which in my opinion must be looked upon as in the highest degree pernicious ; the one may be called the dry plan, the other consists of a dietetic management directly antagonistic to that which has been advocated.

It has been suggested that our efforts should be directed towards controlling the elimination of urine by recommending abstemiousness in the ingestion of fluid. The increased elimination of urine, however, is only a consequence of the disease, and withholding fluids will not affect the essential part of the complaint, which consists of the unnatural passage of sugar into the circulation. It is to the presence of sugar in the circulation and its tendency to escape by the kidney that the large quantity of urine passed is attributable, fluid being carried off with it as it is discharged. To replace the fluid that is thus lost may be considered as fulfilling a physiological requirement, and hence the plan under consideration is directly opposed to rational principle. Thirst affords an indication that fluid is required in the system, and to appease the sensation by drinking is only complying with the dictates of nature. As long as fluids are not taken that are calculated to aggravate the disease by supplying a source for increasing the elimination of sugar, I hold that it is natural and wise that they should be ingested to any extent that may be desired. Both from experience and reasoning I would place no limit upon the amount of fluid that may be consumed, but simply leave it to the patient to quench his thirst whenever thirst is experienced. To curtail him in fluid is to occasion distress; and, at the same time, also, I believe, to place him in a more perilous position: for, the more freely the sugar existing in the system is carried away the less will be the extent of deviation in the contents of the circulatory system from a natural condition. It is indispensable, it must be remembered, that what is drunk should not be of a nature to yield sugar, for should such be the case it would be like adding fuel to fire—the more that was drunk the more desire would there be for drinking.

From what I have myself seen of diabetes mellitus, I cannot understand how any patient suffering from the disease can have been made otherwise than very much worse by the administration of sugar, and yet this has been advanced as a plan of treatment for the complaint.

M. Rigodin, according to what is stated in one of the numbers of the 'Lancet' for January, 1862, proposed the administration of a diet in which sugar-yielding substances enter largely in order to compensate for the loss of sugar that is taking place. Because, from the experiments of Dumas and Bernard, sugar appeared to form an important principle in the animal system, he thought it rational to give sugar in diabetes to make up for the loss occurring as the result of the disease. No comment is needed upon an argument so utterly gratuitous as this.

Some cases are recorded in the 'British Medical Journal' for May 29th, 1858, by Dr. Sloane, in which the saccharine treatment was put into force. It was tried upon three patients in the Leicester Infirmary. In the first, half a pound of treacle a day was given to the patient for more than nine weeks. The urine was increased in quantity it is stated by three quarts a day, being thereby more than doubled, and the sugar rose from fifty-six to eighty grains per fluid-ounce. Upon an opposite plan of treatment being resorted to, the quantity of urine and proportion of sugar soon underwent a marked decline. In the second, sugar was administered for a month : half a pound of treacle during the first three days, and then, the same quantity of honey during the remainder of the time, as the treacle induced nausea, and made the patient feel thirsty. At the end of the month there was much greater weakness, a loss of two and a half pounds in weight, and much greater thirst. The honey was, therefore, ordered to be omitted. The quantity of urine had increased from eight to fourteen pints, but it only contained one grain extra of sugar per ounce. In the third case, half a pound of treacle was given daily from November 28th, 1857, to January 16th, 1858, to a girl fourteen years of age, the subject of the complaint. The patient during the time lost four pounds in weight. An increase of a pint in twenty-four hours took place in the quantity of urine, and the proportion of sugar rose from sixty-four to seventy grains per fluid-ounce. "The girl," continues the report, "was discharged at her own request, and died on February 17th, at her home in the country." Strangely enough, notwithstanding the nature of these results, which form the basis of Dr. Sloane's communication, he finishes by remarking that much has yet to be learned concerning the mode of using sugar in glycosuria, and offers suggestions, as if it had proved a desirable remedy, regarding the kind of sugar to be selected and the mode of administering it.

I have never put the saccharine plan of treatment into practice myself, and knowing what I do about the disease I should not consider myself justified in trying it. I once had an opportunity, however, some years ago, of witnessing its employment upon a case in Guy's Hospital. The patient was rendered so much worse by it that it had to be discontinued in the course of a few days.

Various medicinal agents have been from time to time recommended, suggested by the theory that has happened to be entertained regarding the nature of the disease.

Under the supposition that the production of sugar was due to a faulty action of the digestive organs, pepsine and runnet have been employed, but, as might be inferred from what has been said under the head of pathology, without any beneficial effect. Yeast is also an agent that has been administered with the view of getting rid of the sugar supposed to be unnaturally produced in the stomach. M'Gregor ('Med. Gazette,' May, 1837, p. 272) gave yeast to two patients in ounce doses after each meal, but it had soon to be discontinued on account of the patients feeling, to use their own expression, as though they "were on the eve of being blown up." Such a sensation is just what might be looked for, seeing that the conditions were supplied for the occurrence of the alcoholic fermentation within the stomach.

The permanganate and perchlorate of potash have been employed as oxidizing agents by those who have thought that a defective oxidation of sugar formed the cause of its presence in the system. More recently the peroxide of hydrogen has been used upon the same principle, and this agent has during the last few months attracted a considerable amount of attention from a case that was reported as having been benefited by it, in one of the medical periodicals. I have tried it in a few cases, but without having been able to trace the production of the slightest effect either one way or the other. I believe, from observation, that it is perfectly devoid of power of influencing the disease; and, further, there are no grounds to show that the disease is in any manner connected with defective oxidation or that defective oxidation in reality exists. An analysis of the urine of my patients was made, and no diminution of sugar was noticed.

A *post hoc* must not be taken as constituting a *propter hoc*, and because in one particular case an improvement may be noticed under the employment of an agent it must not be immediately concluded that the effect was due to the agent. There may be other influences in operation to which the result may be attributable. When a patient falls under treatment measures as well as medicines are prescribed by the medical attendant. I think the statement will be endorsed by those who have had experience in hospital practice that, no matter what the medical treatment adopted, and without any change in the character of the diet, diabetes usually show signs of improvement upon the admission of the patient into the wards of an hospital. Early hours, the plainness and wholesomeness of the food, and the regular mode of living, have essentially, I believe, to do with the result. I remember the case of a patient who was some time ago sent to me from the country for admission into Guy's Hospital as a diabetic. His urine was found to be natural in quantity, but to contain a small amount of sugar. He was not placed upon a restricted diet, and only some simple medicine was ordered for him. In the course of a few days his urine was found to be perfectly devoid of sugar, and I cannot help thinking that this event was due purely to an alteration in the hygienic conditions with which the patient was surrounded.

Without reference to any theoretical consideration in explanation, I think it may be concluded that benefit is derivable from the administration of alkalies. It is in the carbonated form that it is desirable to give them, and I am in the habit myself usually of ordering ten, fifteen, or twenty grain doses of the bicarbonate of potash in combination with the aromatic spirit of ammonia.

It is not always possible to prove that a medicinal agent possesses the power that it has the credit of enjoying. General experience, however, in this case tends strongly to justify the conclusion that alkalies exert a controlling influence over the morbid condition prevailing in diabetes. I may mention an instance which not long ago fell under my notice, where a striking exemplification was afforded in support of this conclusion. The case was that of a gentleman, between fifty-five and sixty years of age, the subject of diabetes, whom I had been in the habit of seeing occasionally for some four or five years previously, and who had become so far relieved of his disease that he presented the appearance of enjoying perfect health, and was able to partake of an ordinary mixed diet without experiencing any ill effects. Generally his urine contained only a few grains of sugar to the ounce, and the quantity passed was within about the ordinary range. One day he came to me; and, finding close upon eleven grains of sugar to the ounce, I ordered him a mixture containing the bicarbonate of potash, aromatic spirit of ammonia, and compound tincture of lavender. In his mode of living he was to continue precisely as before. Three days afterwards the sugar had fallen to three and a half grains to the ounce. He was about to get married, and, in consequence of some anxiety that occupied his mind with regard to his generative power, a consultation was held at which I was present. This took place on the following day. It was considered advisable that strychnine and phosphoric acid should be prescribed for him, and, although I had my misgivings about the effect of the acid upon his diabetes, I consented that he might take it with a watch being kept upon the urine. He did so, and four days afterwards I found that the sugar had risen to thirteen and a half grains to the ounce. I now gave him the strychnine in the form of a pill, and directed him to return to the bicarbonate of potash mixture. I saw him again in three days' time, and now the urine contained only a trace of sugar. I could perceive nothing to account for these results besides the influence of the medicinal agents taken.

The effects described in a previous part of this volume as having been produced by the introduction of acids and alkalies into the circulatory system agree with what has just been mentioned. It has been stated that by the injection of carbonate of soda into the circulatory system the production of artificial diabetes, by operating upon the sympathetic, is prevented. A saccharine state of the urine may also be experimentally induced by the introduction of phosphoric acid into the circulation.

From having noticed that the production of artificial diabetes could be prevented by the agency of the carbonate of soda, I some time ago tried the effect of employing it in large doses, and also the vegetable salts of the alkalies, which give rise to the production of a carbonated alkali in the system, in human diabetes. I gave carbonate of soda to the extent of four drachms, acetate of potash six drachms, citrate of potash six drachms, and the tartrate of potash and soda, or rochelle salt one ounce a day, but without observing any decided effect upon the urine. It is from moderate doses and their long continuance that it would seem the good effect of the alkalies in diabetes is to be looked for. It is worthy of remark, as constituting a striking and peculiar circumstance specially belonging to diabetes, that, notwithstanding the administration of the above-mentioned agents in the quantities stated, the urine did not acquire an alkaline character. In one of the cases, after the tartrate of potash and soda had been administered for some time, I took it off, and gave some dilute phosphoric acid instead. The patient was for seventeen days upon the vegetable saline, during which time the sugar passed gave a daily average of 1027 grains. He was also for seventeen days upon the phosphoric acid. The sugar passed gave a daily average amounting to 1409 grains. A restricted diet was being taken all the while.

After the first intensity of the disease has been subdued the alkaline mineral waters come in very usefully for employment. The Vals, Vichy, and Seltzer are the waters to be selected from.

The Vals is the strongest of the class; and of the various springs at Vals the Magdeleine is that which yields the strongest water.

The Vichy waters come next in strength. They have been much longer known than the waters of Vals. The strongest springs are the Hauterive and Célestins. The former is the water most largely exported from Vichy. It is much more highly charged with free carbonic acid than any of the rest. The Mesdames spring furnishes a rather milder water than the two above named. For this reason, and also from the fact of its containing a larger amount of iron, it is better suited for some persons, especially delicate females.

At Vichy there are extensive baths, and invalids, especially diabetics and dyspeptics, flock to the place from all parts during the season, which lasts from the beginning of May to the middle of October. By a three or four weeks' sojourn at Vichy, during which the waters are drunk morning and afternoon, and the baths daily or almost daily had recourse to, much good is often produced. There are many diabetics, in fact, who annually repair to Vichy to be set right for another year. It must be borne in mind, however, that the Vichy water treatment, carried out in full force, does not suit all diabetics. I have known some upon whom it has produced very bad effects, and who have been thereby compelled suddenly to desist from its employment.

The Seltzer water possesses comparatively mild alkaline properties. It is sometimes usefully prescribed for habitual employment as a portion of the fluid consumed through the day.

Each of these waters may be drunk alone, or taken in conjunction with wine or brandy. They may also be employed at meals.

The Carlsbad water, a water belonging to the saline class, is also of service in some cases of diabetes. Where an habitual tendency to constipation, and a sluggishly acting liver, attended with congestion of the portal system, exist, I think the Carlsbad water may be advantageously recommended.

A few weeks' sojourn at Carlsbad also, as in the case of Vichy, is often productive of a considerable amount of benefit.

There is one remedy for diabetes to which I have not yet alluded, and which I believe has not yet received the full trial it deserves. The remedy I refer to is opium. As far back as 1837 M'Gregor placed upon record in the 'London Medical Gazette' a couple of cases which had been treated with this agent. Under its influence the urine underwent a marked diminution, and the symptoms of diabetes became subdued. M'Gregor's cases, however, did not terminate satisfactorily, the disease, it is stated, having returned upon a discontinuance of the employment of the opium. It is a peculiarity belonging to diabetes that patients suffering from the complaint bear doses of opium without the production of any of the ordinary effects that could not be tolerated by a healthy individual. M'Gregor, in his two cases, pretty rapidly increased the dose, until the quantity administered in the twenty-four hours amounted in the one to sixty and in the other to ninety grains. I have myself often begun with a grain three times a day without observing the slightest sign of soporific effect.

I have long been in the habit of administering opium in moderate doses, and, as I conceived, with good effect; but latterly I have pushed it further, and must say have been astonished at the highly successful results that have occurred. I have seen enough to satisfy me that opium exerts a direct remedial effect upon the disease.

In a case that has been under my care in Guy's Hospital during the past summer, and the details of which I purpose laying before the profession through another channel, the patient has been entirely relieved of her disease by the influence, and the influence only, of opium. It is true, being a case occurring at an advanced period of life, the patient being about sixty, it was a favorable one for treatment. She was suffering and had been suffering for some time from the disease in a well-marked form. Opium was given in increasing doses, until the sugar disappeared, which happened when the quantity of opium reached nine grains daily. When it was first taken off, the sugar re-appeared, but after continuing it some time longer it was found that a diminution of the dose led to no return of sugar. The diminution was continued until ultimately all was taken off, and the urine still remained devoid of sugar. For several weeks past the patient has been taking no medicine whatever, and she exhibits no sign of the existence of diabetes. I should add that no restriction in diet from the beginning was practised. The full diet of the hospital—an ordinary mixed one—was ordered for her when she was first admitted, and this she continued to take as long as she remained. I have seen her from time to time since her discharge, with the view of keeping an eye upon the progress of her case, and she informs me that she has been living just as she used to do before she became affected with the complaint. It was only a few days back from the period I am writing that her urine was submitted to examination, and found to be, as when she was discharged from the hospital, devoid of sugar.

Notwithstanding the result here recorded, I do not think that a like relief is to be obtained in all cases without the assistance of a restricted diet. In young subjects the disease assumes a more severe form, and is not so amenable to treatment. That opium, however, here also exerts a marked controlling influence I have had several opportunities of observing. By a restricted diet I have succeeded in reducing the sugar to a certain point, and then by the administration of opium have further succeeded in removing it altogether.

The bowels are often difficult to keep in a properly acting state in diabetes. As a rule there is a tendency to constipation, but not unfrequently the reverse condition is encountered. In some cases there is at one time constipation and at another diarrhœa, so that the patient is harassed with either the one or the other. Where constipation prevails I have sometimes seen much relief—relief beyond that merely attached to the bowels—afforded by the administration of a purgative saline mixture. The Pülna water, if strong enough for the purpose, may be advantageously had recourse to for overcoming constipation.

In the treatment of the incidental complaints that the diabetic may happen to become the subject of, the practitioner must be guided by general principles, but attention requires to be given to secure the exclusion of saccharine and sugar-forming agents from the prescription. In ordering an enema also something must be used in the place of the decoction of starch or barley water—the ordinary vehicles.

Before concluding these remarks upon treatment I may refer to a measure which has been recently advanced as one of great importance by M. Bouchardat, the Professor of Hygiène to the Faculty of Medicine in Paris. Anything coming from such a source upon the subject of diabetes deserves our highest consideration. Bouchardat has long been a strong advocate for strict attention to the dietetic regime which has been recommended in this volume. More recently he has urged that equal attention should be paid to other points of a hygienic nature. He stoutly maintains that a large amount of benefit is producible by active muscular exercise (*exercise forcé*) in the open air every day; and he is in the habit of recommending his patients systematically to attend at a gymnasium, or to subject themselves to some kind of work or exercise sufficiently active to throw them into a good perspiration. By this he is of opinion—and it is a perfectly rational one, for muscular exercise tends to improve the condition of the body, and the more this can be effected the more is the disease found to be controlled—that a return of power of appropriating the starchy and saccharine elements of food is promoted.

Bouchardat further urges that especial care should also be taken to keep the skin warm and dry, and that the patient should be kept in a calm and contented state of mind, without exposure to excess of mental work. To be surrounded, in fact, by perfectly hygienic conditions, such as those which he instances are secured by the training of the pugilist, is what he advocates for the diabetic.

REPORT OF NORTH'S CASE,

SHOWING

THE INFLUENCE OF VARIOUS ARTICLES OF FOOD UPON THE ELIMINATION OF SUGAR IN DIABETES.

Joseph North, æt. 32, a patient under my care in Stephen Ward, Guy's Hospital, at the beginning of 1861. A light-haired, fresh-complexioned man, who, previous to his present complaint, had scarcely known a day's illness to have happened to him. During the commencement of November, 1860, his disease set in; according to his own account, under the following circumstances: He had been drinking to excess, and was suffering from retention of urine, for the relief of which he procured an ounce of the sweet spirit of nitre, and took it in two doses within the space of five hours. He drank copiously afterwards of linseed tea, and in a few days' time noticed that he began to pass an unusual quantity of urine, which continued increasing in amount, until, within a week, it reached, he said, as much as six to seven quarts during the day, and from three to four during the night. He now suffered from much pain in the loins, and found himself rapidly wasting, with a voracious appetite, an insatiable thirst, and a dry skin.

The patient presented the appearance of being a strong-constitutioned man, although he carried with him the characteristic diabetic aspect. He complained of nothing but what was attributable to his special disorder, and there was no evidence of his lungs or other organs being otherwise than perfectly sound; so that he formed an instance of a pure, uncomplicated case of diabetes at a middle period of life. He also possessed an amount of intelligence surpassing what is usually met with in persons of his sphere of life, and with readiness and willingness consented to implicitly carry out whatever instructions might be given him. Time showed that he entered enthusiastically into the spirit of the observations that were being conducted. I was dependent upon him, not only for obedience to my instructions and for giving an exact account of all he partook, but also for attention to the collection of his urine in separate vessels for the several periods into which the twenty-four hours were designedly divided. He was under the surveillance of the attendants and the other patients in the ward, of whom I made inquiries to see if his statements could be relied upon. From the information I obtained, and from the consistency in the results of my examination of his urine, I have the strongest reason to believe that his share in the inquiry may be taken as having been performed with as much exactitude as is well possible to have been observed. In every respect, indeed, I regard him as one of the most desirable persons I could have alighted upon for carrying out the investigation that was conducted.

It may be as well to state that every analysis given in the report was made by myself; but there were two students to whom my thanks were specially due for their assiduous atteution in the case. To Mr. Cookson I was indebted for assistance rendered in the ward, and to Mr. Lamb for assistance rendered in the laboratory. Without exception, the analyses were made from day to day, as soon as the tweuty-four hours had expired, so as to avoid loss of sugar from decomposition. The determination of the quantity of sugar was effected by the cupro-potassic liquid according to the manner elsewhere described.

The object I had in view was to examine as carefully as possible the influence exerted by the common articles of diet over the extent of elimination of sugar—to ascertain, in fact, as closely as I could, the relation existing between the food ingested and the sugar voided by the patient. In order to get the separate effect of his meals, I divided the twenty-four hours into periods of four hours each, and directed him to collect his urine in separate vessels for each. He was always to empty his bladder when the end of the period had arrived, and to be careful that no loss of urine occurred when he had an alvine evacuation. I had thus six specimens of urine for examination every day; and attention was directed to the quantity, specific gravity, extent of saccharine impregnation, and the general appearance of each.

A synopsis of the results obtained will be found arranged in a tabular form further on, with an account of the diet that was from day to day taken.

From the materials furnished by the case a plan has been framed, showing at a glance the influence of different articles of food upon the elimination of sugar. The plan, for the sake of convenience of reference, has been introduced into a previous part of this volume (*vide* p. 238).

In the daily report that follows, I have only selected from the details of the case what I considered to be the principal features of interest. The whole of the results observed being systematically arranged in a tabular form further on, would render it superfluous to do more.

Throughout the period during which the observations were being conducted, the patient took one grain of opium three times a day, which formed the only medicine administered. He was allowed four ounces of brandy and two bottles of soda water *per diem*, and tea without milk or sugar, and water *ad libitum*. For the first few days a full mixed diet was given in order to obtain a starting point for ascertaining the effect of restriction.

February 1st and 2nd.—These tweuty-four hours extended from one o'clock the middle of one day, to one o'clock the middle of the next. The diet was a full mixed one. The amount of sugar passed was 9175 grs.; the amount of urine, 233 oz. The six specimens gave as their mean sp. gr. 1042, and as the mean quantity of sugar per oz. 40·97 grs. On looking at the six specimens placed side by side, it was striking to observe how much darker in colour that passed between one and five in the morning was than either of the rest.

5th.—The twenty-four hours' period was now made to commence from one o'clock in the morning instead of the afternoon, in order to get the effect of each day's diet manifested upon the urine belonging to that day. The reason for passing from the 2nd to the 5th was, that the urine for two days escaped being examined, the system of procedure not having been then definitely marked out.

To-day the patient was upon a full mixed diet. Quantity of sugar 10,573 grs.; quantity of urine 259 oz.; mean sp. gr. of the six specimens of urine 1037; mean amount of sugar per oz. 41·29 grs. The quantity of sugar passed between 1 and 5 a.m. was 593 grs., and between 5 and 9 a.m. 889 grs.; whilst during the remainder of the day it was upwards of 2000 grs. for each four hours. There is thus a striking increase in the extent of production of sugar occasioned by the immediate influence of the meals. The urine passed between 1 and 5 a.m. was of nearly a healthy yellow colour, the other specimens were pale and diabetic looking.

6th.—Full mixed diet again. Quantity of sugar 8961 grs.; quantity of urine, 205¾ oz.; mean sp. gr. 1039; mean amount of sugar per oz., 44·05 grs. As upon the preceding occasions, the urine passed between 1 and 5 a.m. was of a much darker colour than any of the rest.

7th.—To-day the diet was changed, and the patient allowed only to take animal food. He had two mutton chops, 3 oz. dressed meat, and two pints of beef tea. The average weight of the mutton chops supplied in the hospital may be taken from observation at about 7 oz. The quantity of sugar immediately fell to 2474 grs.; quantity of urine only 77¼ oz. The specific gravity for the first two periods of the day was 1043 and 1046; for the last it had descended to 1025. Again, during the first two periods of the day the urine was charged with sugar to the extent of 44·80 and 41·30 grs. per oz.; during the last there was only 20·15 grs. per oz. All the urine now presented a fair amount of colour, and that passed in the afternoon between 1 and 5 threw down a lithate deposit.

8th.—The diet consisted of three chops and three pints of beef tea. Quantity of sugar 3035 grs.; quantity of urine 143 oz. The urine passed between 5 and 9 in the morning was of the highest sp. gr., viz. 1037; that passed between 9 and 1 at night, the lowest, viz. 1013. A corresponding order was noticeable in the degree of saturation with sugar. During the former of the two periods the urine contained 26·35 grs. per oz.; during the latter 13·45.

All the specimens of urine were again pretty fairly coloured, and that passed during the afternoon threw down a deposit of lozenge-shaped crystals of lithic acid.

The patient expressed himself as feeling much less thirsty, and said that during the previous night he had been in a good perspiration, such as he had not been in before for the last three months.

9th.—Two chops, 4 oz. of dressed meat, 1 egg, and 3 pints of beef tea for diet. Quantity of sugar 2471 grs.; quantity of urine 127¼ oz. There was no sp. gr. observed exceeding 1030. The specimen presenting the lowest was again that from 9 to 1 at night. It was 1013, and contained 12·10 grs. of sugar to the oz. In the other specimens the sugar per oz. did not exceed 24·45 grs.

10th.—The diet allowed was 1 chop, 1 lb. of dressed meat, 1 egg, and 3 pints of beef tea; but the patient took also, at 4 p.m., a pint of prepared cocoa sweetened with sugar. It was Sunday afternoon, and his friends had been to see him and brought him this as a treat. Henceforth, he was stringently directed not to have anything brought in, and watch was put upon him to see that it was carried out. Quantity of sugar passed 3179 grs.; quantity of urine 136 oz. It was exceedingly interesting to look at the amount of sugar passed during the different periods of the day, and notice the immediate effect produced by the violation of his instructions that he committed. From 1 to 5 a.m. it was 290 grs.; 5 to 9 a.m. 166 grs.; 9 to 1 p.m. 461 grs.; 1 to 5 p.m. 468 grs.; 5 *to* 9 *p.m.* 1311 *grs.*, and 9 to 1 a.m. 483 grs. He partook of the sweetened cocoa at 4 p.m.

Between 1 and 5 p.m. the sugar was as nearly as possible the same as during the preceding four hours. But between 5 and 9 p.m. he passed upwards of 800 grs. more than he might have fairly been expected to have done, had he not departed from his prescribed regimen. During the following four hours the amount fell to nearly what it was before the rise. It thus seems that what was taken at 4 p.m. manifested its principal effects between 5 and 9 p.m., and that the sugar the result of ingestion was all carried off, or had, so to speak, filtered through the system and been discharged, by the end of this time. The urine, which had been previously more or less high coloured, became during the last two periods of the day almost as colourless as water.

11th.—One chop, 13 oz. of dressed meat, and 3 pints of beef tea for diet. Quantity of sugar passed 3329 grs.; quantity of urine 140¼ oz. It appeared as if his infraction of the previous day had still left traces of its ill effects for several hours. The sugar continued high in quantity up to 5 p.m. to-day. Between 1 and 5 p.m., in fact, he passed 1016 grs.; the urine having a sp. gr. of 1035, and containing 33·30 grs. of sugar to the oz. From 5 to 9 p.m., the amount of sugar was 418 grs.; and during the next four hours only 200 grs. This last urine was of a sp. gr. 1013, and contained 7·40 grs. of sugar to the oz.

12th.—Diet, 1 pair small soles, 1 chop, 4 oz. of dressed meat, and 3 pints of beef tea. Quantity of sugar 1096 grs.; quantity of urine 92¾ oz. The last specimen of urine—that passed between 9 and 1 at night, was again of a sp. gr. 1013, and contained only 6 grs. of sugar to the oz. The highest degree of saturation with sugar attained to-day was 19·35 grs. to the oz. Some of the urine again deposited lithates and lithic acid.

13th.—The diet consisted of fish and beef tea only. Four pairs of small soles and 2 pints of beef tea were consumed. Quantity of sugar 1696 grs.; quantity of urine 163 oz. The quantity of sugar per oz. did not reach higher than 15·15 grs., and for the last period of the twenty-four hours descended to 5·83 grs. Three of the specimens of urine threw down crystals of lithic acid.

14th.—Diet, 2 pints of jelly, 16 oz. of dressed meat, and 1 pint of beef tea. The jelly was made in the usual way, and flavoured with sugar, a little sherry, and essence of lemon. Quantity of sugar passed 952 grs.; quantity of urine 107½ oz. The sugar in the jelly, of which I was informed 2 oz. were allowed for the 2 pints, evidently exerted a deleterious tendency. The jelly was all taken at 6 and 9 in the morning, and no other food till 1 p.m. Between 9 and 1 in the day, the urine presented a sp. gr. of 1031, and contained 25·25 grs. of sugar to the oz. During the other portions of the day, the amount of sugar per oz. was not higher than 13·15 grs., and during the last two periods was only 3·33 and 3·69 grs. respectively.

15th.—Diet, two pints of jelly, two chops, and two pints of beef tea. Quantity of sugar passed, 569 grs.; quantity of urine, 107¾ oz. The jelly to-day was made without sugar. One pint of it was taken at 6 a.m., and the other at 10 a.m., with no other food till 1 p.m. The sugar passed was infinitely lower in quantity than it had ever been noticed before. The proportion per ounce of urine did not exceed 7·56 grs., and the lowest was 2·35. The sugar voided during the respective periods of the twenty-four hours was 76, 30, 56, 86, 67, and 254 grs. Looking at these figures, it would appear that jelly does not occasion so much production of sugar as meat. Up to 1 p.m. nothing but the jelly was taken; and after 1 p.m. the meat and beef tea. The amount of sugar continued exceedingly low up to 9 p.m., but during the succeeding four hours the quantity was 254 grs.—nearly half of the amount given for the twenty-four hours. I presume this may be taken as the effect of the change to meat, and that the sugar resulting from the ingestion of meat requires a longer time to make its appearance in the urine than that resulting from the ingestion of saccharine and starchy materials. The patient confidently stated to-day to the reporter of his case, that he felt certain that he was getting better on account of a particular symptom he had observed. To use his own words, " He had been like a child hitherto during his illness but now he found that the nature of man had returned upon him." His weight to-day was 9 st. 5 lbs.

16th.—Diet, one chop, sixteen ounces of dressed meat, and three pints of milk instead of the beef tea. Quantity of sugar, 1198 grs.; quantity of urine, 105½ oz. The lowest amount of sugar per ounce noticeable to-day was 7·65, which is a trifle higher than the highest of yesterday—a fact that presents a significant appearance with respect to the substitution of milk for beef tea.

17th.—Diet precisely the same as yesterday. The amount of sugar passed was 1258 grs.; quantity of urine 98¼ oz. Mean sp. gr. of the six specimens 1026. Mean amount of sugar per oz. 14·96 grains. The patient stated that a much less amount of food satisfied him now than formerly, and that he did not experience thirst as he used to do.

18th.—Diet the same as yesterday, with the addition of half a pound of suet, which was mixed with the milk. Quantity of sugar, 1485 grs.; quantity of urine, 99½ oz. Mean sp. gr. given by the six specimens, 1025. Mean amount of sugar per ounce, 16 95 grs.

19th.—Diet, two chops, eight ounces of dressed meat, three pints of milk, and three quarters of a pound of suet. Quantity of sugar, 1722 grs.; quantity of urine, 83¾ oz. Mean sp. gr. of the six specimens, 1031. Mean amount of sugar per ounce, 21·62 grs.

20th.—Diet, one chop, sixteen ounces of dressed meat, three pints of milk, and a quarter of a pound of suet. Quantity of sugar, 2225 grs.; quantity of urine, 101½ oz. Mean sp. gr. of the six specimens, 1033. Mean amount of sugar per ounce, 23·47 grs.

According to the patient's opinion—and he had not been informed of the analytical results obtained—the milk he was having did not agree with his complaint; for since he had been taking it, he began to experience somewhat similar sensations to those he had at the commencement of his disease. He liked the suet, and said it filled up the void which seemed to exist at the pit of the stomach more than anything else he had yet taken. In strict accordance with the statement that was expressed by the patient, the condition of his urine had been steadily getting worse, during the whole period (five days) that he had been supplied with milk. It is true, during the latter three days he had also been supplied with suet; but the effect observed would not appear to be due to this; for, the last day, when there was a rise of 500 grs. of sugar, he only had a quarter of a pound of suet; whilst on the day previously he took three quarters of a pound, and the day before that half a pound.

21st.—Diet, six eggs, one pound of dressed meat, and two pints of beef tea. The quantity of sugar descended to 927 grs., and the amount of urine to 65 oz. Three of the specimens of urine again deposited crystals of lithic acid.

The patient's weight to-day was 9 st. 5 lbs., being exactly the same as when he weighed on the 15th.

22nd.—Diet, eight eggs, two chops, and two pints of beef tea. The quantity of sugar again fell, amounting only to 734 grs. The quantity of the urine was 71¾ oz. Some of the urine threw down lithates and crystals of lithic acid.

23rd.—Diet, four dozen oysters, one pound of dressed meat, and three pints of beef tea. Quantity of sugar, 1310 grs.; quantity of urine, 115¾ oz.

24th.—Diet precisely the same again as yesterday; but the quantity of sugar was only 896 grs., and the quantity of urine 97 oz. Looking to these two days' results, the effect of oysters upon the production of sugar in the complaint is not very clear. I had expected to find the amount of sugar increased on account of the considerable quantity of amyloid substance which the oyster contains, and this expectation was realised by the first day's examination; but on the second day the sugar fell to quite a moderate degree. Between 1 and 5 in the afternoon, the four hours' urine only contained 16 grains, and was charged merely to the extent of 2·4 grains in the ounce. The oysters had been all taken at 7 o'clock in the morning, and throughout the day until night the sugar continued low.

25th.—Diet, one chop, eight ounces of dressed meat, and three pints of beef tea. Quantity of sugar, 867 grs.; quantity of urine, 78¼ oz.

26th.—Diet, eight ounces of suet, three chops, and three pints of beef tea. Quantity of sugar, 876 grs.; quantity of urine, 103 oz.

Between 1 and 5 p.m. the urine that was passed only contained a trace of sugar. This was the first time that I had noticed any specimen in such a state.

The suet was given with only meat and beef tea, to clear up the point that was left unsettled when it had been given with milk. The result obtained clearly showed, as had been surmised, that the rise before observed was not due to the suet.

27th.—Diet, four ounces of gum arabic made into a dilute mucilage, and drunk at intervals during the morning, one chop, one pound of dressed meat, and two pints of beef tea. The quantity of sugar ascended from 886 to 1177 grs.; the amount of urine was 95 oz.

The patient weighed to-day 9 st. 10 lbs., being an increase of 5 lbs. since the 21st.

28th.—Diet, one chop, one pound of dressed meat, and three pints of beef tea; the same diet as yesterday, substituting one pint of beef tea for the four ounces of gum. The quantity of sugar descended, returning to 887 grs. The amount of urine was 71½ oz. The specimen passed between 1 and 5 p.m. threw down lithates.

March 1st.—Diet, three chops, greens, and two pints of beef tea. Quantity of sugar 594 grs.; quantity of urine, 65½ oz.

For the second time, one of the specimens of urine contained a trace of sugar only; and, as on the previous occasion, it was the urine passed between 1 and 5 in the afternoon. Once before, there was a particularly small quantity of sugar (sixteen grains) eliminated for the four hours, viz., on February 24th; and this also occurred during the period from 1 to 5 p.m.

Four of the specimens to-day deposited lithates.

2nd.—Diet, seventeen ounces and a half of bran biscuits, one chop, one pound of dressed meat, and three pints of beef tea. The quantity of sugar rose to 2630 grs.; amount of urine, 96½ oz. The bran biscuits were commenced at 6 a.m.; and even the urine passed between 5 and 9 a.m. bore evidence of their effects, for the amount of sugar per ounce sprang from 15·99 grs. to 29·37, and continued higher than this till 9 p.m., when it made a slight descent to 26·64 grs.

The patient soon perceived in his bodily sensations the prejudicial effect of his alteration of diet. About the middle of the day he said he did not know how the bran biscuits would suit him, but he thought they made him thirsty, and his mouth dry.

3rd.—Diet, twelve ounces of bran biscuits, one chop, one pound of dressed meat, and three pints of beef tea. Quantity of sugar passed, 3291 grs.; quantity of urine, 110¼ oz. The proportionate amount of sugar in the urine fluctuated between 22·50 and 36 grs. per ounce, and the sp. gr. between 1030 and 1043.

The patient felt quite sure the bran biscuits were not agreeing with him; for not only was he thirsty, and his mouth dry, but the skin of his hands, instead of being supple as it had lately been, was dry and harsh.

4th.—Diet, twelve ounces of gluten bread, one chop, twelve ounce of dressed meat, and three pints of beef tea. Quantity of sugar passed, 4079 grs.; quantity of urine, 151 oz. The proportion of sugar in the urine fluctuated between 23·58 and 30·63 grs. per ounce, and the sp. gr. between 1031 and 1038.

5th.—Diet, five ounces and a half of gluten bread, three chops, four ounces of dressed meat, and three pints of beef tea. It will be observed that five ounces and a half of gluten bread were taken to-day, instead of twelve as yesterday. The quantity of sugar fell to 3228 grs., and the quantity of urine to 121½ oz. The proportion of sugar in the different specimens of urine ranged between 19·71 and 31·29 grs. per ounce. The gluten bread that was taken, was eaten, a portion at 10 a.m., and the remainder at 1 p.m. On the three previous days the gluten bread and bran biscuits were commenced with the patient's breakfast, at 6 a.m. Now, it is interesting to notice that to-day there is a successive fall in the sugar passed during the first three periods, and that it is not till between 1 and 5 p.m. that the rise takes place; whilst on the three preceding days, in each case, there is a diminution from the first to the second period, but at the third, viz., between 9 a.m. and 1 p.m., a rise takes place. As there were four hours' difference in the time at which the vegetable aliment was commenced in the day, so there was four hours' difference in the time at which the escape of sugar began to show an increase.

Weight of the patient to-day, 9 st. 10 lbs., which is the same as when he last weighed.

6th.—Diet, one chop, one pound of dressed meat, and three pints of beef tea. The quantity of sugar showed a descent to 751 grs., and the urine to 52¾ oz. The proportion of sugar did not range higher than between 11·70 and 18·45 grs. per oz. Some of the urine again began to deposit lithates.

The patient expressed himself as already feeling better for the omission of the bran biscuits and gluten bread.

7th.—Diet, the same as yesterday. Quantity of sugar passed 11·88 grs.; the proportion of sugar in the six specimens ranging between 9·39 and 18·93 grs. per oz. The quantity of urine was 82¼ oz.

8th.—A return to gluten bread was made, in order to determine as clearly as possible its comparative merit, as placed by the side of the bran biscuit. Fourteen ounces of gluten bread were taken, with three chops and three pints of beef tea. The quantity of sugar immediately rose to 34·43 grains for the day. The amount of urine was 129¼ oz. The urine passed beeween 1 and 5 a.m. contained 12·96 grs. of sugar to the ounce. The gluten bread was commenced at 6 a.m., and the urine passed between 5 and 9 a.m. contained 28·23 grains of sugar to the ounce. The proportion continued high throughout the remainder of the day.

9th.—Diet, fourteen ounces of gluten bread, one chop, one pound of dressed meat, and three pints of beef tea. Quantity of sugar passed, 4539 grs.; quantity of urine, 172¾ oz. The proportion of sugar fluctuated between 23·22 and 30·63 grs. per ounce. All the specimens of urine were pale and diabetic looking. The patient experienced much thirst and dryness of skin.

On reverting to the effect of gluten bread, as compared with bran biscuit, we observe that when, on March 2nd, seventeen ounces and a half of bran biscuits were consumed, the quantity of sugar passed was 2630 grs. On the following day, twelve ounces were taken, and the amount of sugar was 3291 grs. March 4th, gluten bread was substituted in equal quantity for the bran biscuit; the sugar passed was 4079 grs. March 5th, only five ounces and a half of gluten bread were given; the sugar was still 3228 grs. Two days of animal diet were allowed to intervene for the sugar to fall, and gluten bread was again given to the extent of fourteen ounces each day for a couple of days. On the first day the rise was to 3443 grs., and on the second to 4539. These figures would certainly seem to indicate bran biscuit as less objectionable in the way of producing sugar than gluten bread.

10th.—Diet, one chop, one pound of dressed meat, and three pints of beef tea. Quantity of sugar passed, 1726 grs.; quantity of urine, 88¼ oz. Some of the urine again deposited lithates.

11th.—Diet, the same as yesterday. Quantity of sugar, 994 grs.; quantity of urine 86 oz. The proportion of sugar per ounce of urine varied between 9·60 and 16·74 grs. Some of the urine deposited lithates.

12th.—Diet, four ounces of rice, one egg, two chops, and three pints of beef tea. Quantity of sugar, 2587 grs.; quantity of urine, 107 oz.

The rice was taken in the form of a pudding, with the egg; half of it at 6 a.m., and the remainder at 10 a.m. No other food was taken till 1 p.m. Between 1 and 5 a.m. the amount of sugar passed was 81 grs., and its proportion per ounce

13·56 grs. Between 5 and 9 a.m. the figures given were 576 grs. and 28·80 grs.; and between 9 a.m. and 1 p.m., 837 grs. and 31·29 grs. After this, the gross amount descended to 375 grs., but the proportion continued the same. In the following period there was a descent in both, and in the last the proportion was down to 13·98 grs. The rice, then, produced evident effects upon the urine within the period that it was taken; and its influence did not become exhausted until quite the end of the day.

13th.—Diet, one pound of potatoes, one chop, one pound of dressed meat, and three pints of beef tea. Quantity of sugar passed, 2270 grs.; quantity of urine, 102¼ oz. The potatoes were eaten for breakfast at 6 a.m., and nothing else was taken till 11. From 1 to 5 in the morning the gross amount of sugar voided was 281 grs., and its proportion 18·45 grs. to the ounce of urine. Between 5 and 9 a.m. the gross amount rose to 794 grs., and the proportion per ounce to 24·81 grs. During the next period the proportion still showed a rise to 31·29 grs., but it afterwards in each period fell until the last, when it stood at 14·52. After the rise mentioned in the gross amount, there was a successive descent throughout the day till 9 in the evening.

In order that a fair comparison may be made between potatoes and food of a dry description, one pound of potatoes was well dried, and it was found that it lost eleven ounces in weight. The sixteen ounces, then, only contained five ounces of solid matter.

The patient's weight to-day was 9 st. 13 lbs., being a gain of three pounds since March 5th.

March 14th.—Diet, two ounces of arrowroot, one chop, sixteen ounces of dressed meat, and three pints of beef tea. One ounce of the arrowroot was taken at 6 a.m., and the other ounce at 9 a.m., with no other food till 11. Quantity of sugar passed, as nearly as possible, the same as yesterday, viz., 2278 grs.; quantity of urine also nearly the same, viz., 101 oz. It will be observed that the arrowroot was taken at 6 and 9 a.m., instead of altogether at 5 a.m., as with the potatoes. The rise of sugar for the several periods was, in accordance, less rapid. The figures, given in their order for the six specimens throughout the twenty-four hours, run thus—219, 360, 458, 540, 372, and 329 grs. The proportion of sugar to the ounce of urine in the several specimens was 18·21, 30, 32·70, 25·71, 24·81, and 12·18 grs.

15th.—Diet, four ounces of bread, three chops, and three pints of beef tea. Quantity of sugar, 3521 grs.; quantity of urine, 131 oz. The four ounces of bread were taken at 6 a.m. It did not appear to manifest its full effect upon the urine so rapidly as the other articles from the vegetable kingdom that had been given; neither did the effect, when produced, pass off so rapidly. The day began with the patient's passing 197 grs. of sugar during the first four hours, the urine containing 11·79 grs. of sugar to the ounce. From 5 to 9 a.m. the gross amount of sugar was 387 grs., and the proportion 27·15 grs. per ounce. From 9 a.m. to 1 p.m. the figures given were 800 and 31·98; from 1 to 5 p.m., 790 and 35·10; from 5 to 9 p.m., 705 and 30; and from 9 p.m. to 1 a.m., 612 and 22·14. It is thus evident that, although the bread was eaten at 6 o'clock in the morning, its influence was strikingly manifest till the end of the day; and even during the first four hours on the following morning, the amount of sugar was 337 grs., the proportion of sugar to the ounce of urine being 22·50 grs.

As compared with the bran biscuit and gluten bread, the analytical results obtained show that the ordinary bread produces by far a much more prejudicial effect upon the complaint. This will be seen by reverting to the figures, and bearing in mind the difference in the quantity of the articles taken.

16th.—Diet, two pounds of carrots, one chop, one pound of dressed meat, and three pints of beef tea. Quantity of sugar passed 2371 grs.; quantity of urine 91 oz. The carrots were taken in equal portions at 6 and 9 a.m., with an exclusion of other food till 11. The figures representing the gross amount of sugar passed during the six periods of the day, with the proportion of sugar to the ounce of urine, stand thus: 337, 22·50; 346, 28·80; 198, 21·81; 443, 27·69; 375, 31·29; 672, 24.

One pound of carrots, on being well dried, left a residue slightly over three and a half ounces.

17th.—To-day the patient was put back upon a full mixed diet, the same as he had at the commencement of the observations on his case. The amount of sugar rose to 8319 grs., and the amount of urine to 257¾ oz.

18th.—Full mixed diet. Quantity of sugar 8959 grs.; quantity of urine 255 oz.

19th.—Full mixed diet. Quantity of sugar 8355 grs.; quantity of urine 242¼ oz. The amount of sugar per ounce in the various specimens did not fall below 30·75 grs., nor the sp. gr. below 1031.

Weight of the patient to-day 9 st. 12 lbs., which is one pound less than when he last weighed on the 13th instant.

20th.—Full mixed diet. Quantity of sugar 8965 grs.; quantity of urine 247 oz. Taking the six specimens of urine, the amount of sugar per ounce varied between 33·65 and 39·30 grs., and the sp. gr. between 1036 and 1041.

The patient had now been four days on the ordinary full mixed diet of the hospital, and the amount of sugar he passed had fluctuated between 8319 and 8965 grs. per diem. This is not so much, although the diet was the same as when his case was commenced with; for then, during the three days given, the sugar was 8961 grs. at its lowest, and 10573 grs. at its highest. Such a result would tend to show that some permanent improvement, as well as a temporary alleviation, had been obtained by the reduction of sugar for a time through the alteration of diet.

It is curious to notice the successive rise and fall that has occurred in the amount of sugar passed during one day and another under the mixed diet; and, also, under the purely animal diet, when the opportunity was afforded, by its continuance for a few consecutive days together. This is rendered strikingly apparent on referring to the plan (opposite p. 238) that gives a general view of the case, and directing the attention to that part of it corresponding to the first six and the last seven days.

21st.—Diet, one chop, one pound of dressed meat, and three pints of beef tea. An immediate fall was observed in the amount of sugar, from 8965 to 1962 grs., and in the amount of urine from 247 to 80 oz.

22nd.—Diet, three chops and three pints of beef tea. Quantity of sugar passed

1330 grs.; quantity of urine 84 oz. One of the specimens of urine threw down a lithate deposit.

23rd.—Diet, one chop, one pound of dressed meat, and three pints of beef tea. Quantity of sugar 2113 grs.; quantity of urine 97¾ oz.

Having carried my investigations thus far, I now resolved to keep my patient upon animal food, and try if I could discover any medicine that would effect a further reduction of sugar. With this view he remained in the hospital under my care till May 31st. I at first administered large doses of the phosphoric acid, then the carbonate of soda, and afterwards the tartrate of potash and soda. From neither, can I say, I obtained evidence of what would enable me to speak of as marked influence either one way or the other. It is worthy of remark that, although at one time as much as an ounce a day of the tartrate of potash and soda was being administered, yet the urine remained decidedly acid.

Under the animal diet that was thus continued, the patient strikingly improved in bodily appearance, health, and strength. He did not object to his food, did not get tired of it, and said he felt no longing after bread nor any other vegetable substance. He was allowed greens, however, every day. Before he left the hospital he expressed himself as feeling well in every respect. He had never, he said, felt better in his life. He had no thirst, no dryness of skin, and his appetite was easily satisfied. He looked plump in the face as compared with what he had previously done, and wore a happy expression upon his countenance in the place of that abject, pinched-up, miserable, downcast look which he once had, and which is so characteristic of the inveterate form of diabetes. He had been gaining flesh, as is shown by the following return of his weight. The last weight mentioned is for March 19th, when it was 9 st. 12 lbs. April 2nd, he weighed 10 st. 1 lb.; April 16th, 10 st. 4 lbs.; April 23rd, 10 st. 8 lbs.; April 30th, 10 st. 10 lbs.; and when he left the hospital, May 31st, 10 st. 8 lbs. He told me he had reached 11 st., but during the hot weather of the last three weeks in May, he lost 6 lbs. The following is a report of the state of his urine during the last four days he remained in the hospital. He was then upon meat, beef tea, greens, and brandy and soda water, and without medicine of any description. It will be seen that the amount of sugar continued to be about the same as what he had passed under similar circumstances before.

Date.	Quantity of urine in oz.	Sp. gr.	Amount of sugar per oz. of urine in grs.	Total amount of sugar per diem in grs.
May 28th	62	1035	18·	1116
„ 29th	54	1033	17·76	959
„ 30th	58	1034	19·44	1127
„ 31st	56	1036	18·	1008

Tabular representation showing the results produced by the ingestion of various articles of food in the case of JOSEPH NORTH, *æt.* 32, *a diabetic.*

Date.	Period of day.	Sp. gr. of urine.	Quantity of urine in oz.	Quantity of sugar per oz. of urine in grs.	Quantity of sugar in the urine per 4 hrs. in grs.	Quantity of sugar in the urine per 24 hrs. in grs.	Diet taken, with 4 oz. of brandy and 2 bottles of soda water daily, and 1 gr. of opium three times a day. Tea (without sugar), and water ad libitum.	REMARKS.
Feb. 1	1 to 5 p.m.	1045	50	42·36	2118	9475	12.30 p.m., $1\frac{1}{2}$ pint soup (meat and vegetable), bread 2 oz. 4 p.m., bread 5 oz., 1 egg, butter $\frac{1}{2}$ oz. 8 p.m., 1 egg, milk $\frac{1}{2}$ pint, cocoa 10 p.m., 3 oranges	All the specimens of urine were very pale-coloured, except that from 1 to 5 a.m., which was nearly of a natural yellow colour.
	5 to 9 p.m.	1041	61	42·	2562			
	9 to 1 a.m.	1040	49	35·10	1720			
	1 to 5 a.m.	1042	29	42·	1218			
Feb. 2	5 to 9 a.m.	1039	24	42·36	1017		6 a.m., bread 5 oz., milk $\frac{1}{2}$ pint, cocoa, butter $\frac{1}{2}$ oz. 10 a.m., meat 8 oz., bread 4 oz.	
	9 to 1 p.m.	1045	20	42·	840			
Feb. 5	1 to 5 a.m.	1042	14	42·36	593	10573	6 a.m., bread 8 oz., butter $\frac{1}{2}$ oz., milk $\frac{1}{2}$ pint, cocoa 11 a.m., bread 1 oz., meat 4 oz., 1 orange 1 p.m., $1\frac{1}{2}$ pint soup (meat and vegetable) 2 p.m., 1 orange 4 p.m., bread 7 oz., butter $\frac{1}{2}$ oz., 1 egg, milk $\frac{1}{2}$ pint, cocoa 6 p.m., 1 orange 8 p.m., 1 egg, milk $\frac{1}{2}$ pint 9 p.m., 1 orange	The specimen of urine from 1 to 5 a.m. was of nearly a natural yellow colour, that from 5 to 9 a.m. also presented a slight yellow tinge, but all the remaining specimens were nearly as colourless as water.
	5 to 9 a.m.	1039	21	42·36	889			
	9 to 1 p.m.	1035	47	43·62	2050			
	1 to 5 p.m.	1039	$53\frac{1}{2}$	40·	2140			
	5 to 9 p.m.	1034	61	40·70	2482			
	9 to 1 a.m.	1036	$62\frac{1}{2}$	38·70	2419			
Feb. 6	1 to 5 a.m.	1041	26	42·10	1094	8961	6 a.m., bread 8 oz., butter $\frac{1}{2}$ oz., 1 egg 11 a.m., bread 4 oz., meat 2 oz. 1 p.m., $1\frac{1}{2}$ pint soup (meat and vegetable), bread 2 oz. 4 p.m., bread 8 oz., 1 egg, milk $\frac{1}{2}$ pint, butter $\frac{1}{2}$ oz. 8 p.m., 1 egg, milk $\frac{1}{2}$ pint, cocoa	The specimen of urine from 1 to 5 a.m. was of nearly a natural yellow colour, that from 5 to 9 a.m. also presented some amount of colour; the remaining specimens were diabetic looking.
	5 to 9 a.m.	1041	$21\frac{1}{2}$	46·10	991			
	9 to 1 p.m.	1040	$30\frac{1}{2}$	47·	1433			
	1 to 5 p.m.	1010	36	45·30	1631			
	5 to 9 p.m.	1035	64	41·	2624			
	9 to 1 a.m.	1039	$27\frac{3}{4}$	42·80	1188			

Feb. 7	1 to 5 a.m.	1043	11	14·80	627	2474	6 a.m., 1 mutton chop (weight 7 oz.) 9 a.m., beef tea 1 pint 12.30 p.m., 1 chop 6 p.m., dressed meat 3 oz. 7.30 p.m., beef tea 1 pint	The specimen of urine from 5 to 9 a.m. was of a natural yellow colour, a shade paler than this, came that from 9 a.m. to 1 p.m., and next, that from 1 to 5 a.m.; but all the specimens were pretty fairly coloured. The urine passed between 1 and 5 p.m. threw down a considerable amount of pale lithate deposit.
	5 to 9 a.m.	1046	12	14·30	495			
	9 to 1 p.m.	1042	9	28·20	254			
	1 to 5 p.m.	1046	7¼	28·90	217			
	5 to 9 p.m.	1035	20	29·20	584			
	9 to 1 a.m.	1025	14¾	20·15	297			
Feb. 8	1 to 5 a.m.	1032	14	23·05	323	3035	6 a.m., 1 chop 9 a.m., beef tea 1 piut 12.30 p.m., 1 chop, beef tea 1 pint 6 p.m., 1 chop 8 p.m., beef tea 1 pint	All the specimens of urine were pretty fairly coloured, but that passed between 5 and 9 a.m. was more highly coloured than the rest. The urine from 5 to 9 p.m. presented the least amount of colour. That belonging to 1 to 5 p.m. threw down a deposit of lozeuge-shaped crystals of lithic acid.
	5 to 9 a.m.	1037	9	26·35	237			
	9 to 1 p.m.	1023	29½	24·40	709			
	1 to 5 p.m.	1030	23	24·	552			
	5 to 9 p.m.	1025	42½	20·65	878			
	9 to 1 a.m.	1013	25	13·45	336			
Feb. 9	1 to 5 a.m.	1029	11	23·05	254	2471	6 a.m., 1 chop 9 a.m., beef tea 1 pint 12.30 p.m., 1 chop, beef tea 1 pint 4 p.m., 1 egg 7 p.m., dressed meat 4 oz. 8 p.m., beef tea 1 pint	The specimen of urine from 5 to 9 a.m. was the highest coloured, and that from 9 p.m. to 1 a.m. the palest.
	5 to 9 a.m.	1030	15	20·65	310			
	9 to 1 p.m.	1029	21¾	21·80	474			
	1 to 5 p.m.	1030	21½	24·45	526			
	5 to 9 p.m.	1025	26	20·	520			
	9 to 1 a.m.	1013	32	12·10	387			
Feb. 10	1 to 5 a.m.	1023	15	19·35	290	3179	6 a.m., 1 chop 9 a.m., beef tea 1 pint 1 p.m., meat 5 oz. 4 p.m., 1 pint prepared cocoa sweetened with sugar, 1 egg 6 p.m., beef tea 1 pint 7 p.m., meat 6 oz. 8 p.m., meat 5 oz., beef tea 1 pint	The specimen of urine from 1 to 5 a.m. was the highest coloured; those from 5 to 9 p.m. and 9 p.m. to 1 a.m. were almost destitute of colour. * It is to be remarked that the patient to-day departed from his instructions, in partaking of cocoa, sweetened with sugar, at 4 p.m.
	5 to 9 a.m.	1039	5	33·30	166			
	9 to 1 p.m.	1039	15	30·75	461			
	1 to 5 p.m.	1022	27	17·35	468			
	5 to 9 p.m.	1026	47	27·90	*1311			
	9 to 1 a.m.	1018	27	17·90	483			
Feb. 11	1 to 5 a.m.	1027	35½	21·40	760	3329	6 a.m., 1 chop 8 a.m., beef tea 1 pint 1 p.m., meat 7 oz. 2 p.m., beef tea 1 pint 4 p.m., meat 2 oz. 7 p.m., meat 4 oz. 8 p.m., beef tea 1 pint	The specimen of urine from 5 to 9 a.m. was the highest colonred; those from 1 to 5 p.m. and 9 p.m. to 1 a.m. presented very little colour.
	5 to 9 a.m.	1033	13¾	26·65	366			
	9 to 1 p.m.	1032	18½	30·75	569			
	1 to 5 p.m.	1035	30⅓	33·30	1016			
	5 to 9 p.m.	1036	15	27·90	418			
	9 to 1 a.m.	1013	27	7·40	200			

Date.	Period of day.	Sp. gr. of urine.	Quantity of urine in oz.	Quantity of sugar per oz. of urine in grs.	Quantity of sugar in the urine per 4 hrs. in grs.	Quantity of sugar in the urine per 24 hrs. in grs.	Diet taken, with 4 oz. of brandy and 2 bottles of soda water daily, and 1 gr. of opium three times a day. Tea (without sugar), and water ad libitum.	REMARKS.
Feb. 12	1 to 5 a.m.	1032	15	19·35	290	1096	6 a.m., 1 pair small soles 10 a.m., beef tea 1 pint 12.30 p.m., 1 chop 4 p.m., meat 4 oz. 6 p.m., beef tea 1 pint 8 p.m., beef tea 1 pint	The specimen of urine from 5 to 9 a.m. was the highest coloured, and that from 9 p.m. to 1 a.m. the palest. A deposit of lithates occurred in the urine passed between 9 a.m. and 1 p.m. The specimens from 1 to 5 p.m., 5 to 9 p.m., and 9 p.m. to 1 a.m., threw down a crystalline deposit, which proved to consist of lithic acid.
	5 to 9 a.m.	1035	8¾	19·35	169			
	9 to 1 p.m.	1033	13½	16·20	219			
	1 to 5 p.m.	1022	17	7·40	126			
	5 to 9 p.m.	1027	9	12·75	115			
	9 to 1 a.m.	1013	29½	6·	177			
Feb. 13	1 to 5 a.m.	1022	27½	12·75	351	1696	6 a.m., 1 pair small soles 10.30 a.m., 1 pair small soles 12.30 p.m., 1 pair small soles 1 p.m., beef tea 1 pint 4 p.m., 1 small sole 6 p.m., 1 small sole 8 p.m., beef tea 1 pint	The specimen of urine from 5 to 9 a.m. was the highest coloured, and that from 9 p.m. to 1 a.m. the palest. A crystalline deposit of lithic acid occurred in the urine from 1 to 5 a.m., 5 to 9 a.m., and 9 a.m. to 1 p.m. * The sp. gr. of this specimen inadvertently escaped being taken.
	5 to 9 a.m.	1030	20½	15·15	311			
	9 to 1 p.m.	1025	17	12·60	214			
	1 to 5 p.m.	1030	26	14·45	376			
	5 to 9 p.m.	1019	23	6·85	158			
	9 to 1 a.m.	*—	49	5·83	286			
Feb. 14	1 to 5 a.m.	1026	17½	13·	227	952	6 a.m., jelly 1 pint[1] 9 a.m., jelly 1 pint[1] 1 p.m., meat 10 oz. 6 p.m., meat 6 oz. 8 p.m., beef tea 1 pint	The specimen of urine from 5 to 9 a.m. was the highest coloured, that from 5 to 9 p.m. scarcely coloured at all.
	5 to 9 a.m.	1025	12½	13·15	164			
	9 to 1 p.m.	1031	10	25·25	252			
	1 to 5 p.m.	1025	13	9·	117			
	5 to 9 p.m.	1011	27½	3·33	92			
	9 to 1 a.m.	1013	27	3·69	100			
Feb. 15	1 to 5 a.m.	1022	16½	4·61	76	569	6 a.m., jelly 1 pint[2] 10 a.m., jelly 1 pint[2] 1 p.m., 1 chop, beef tea 1 pint 8 p.m., 1 chop, beef tea 1 pint	The specimen of urine from 5 to 9 a.m. was high coloured, and the others moderately coloured, except that from 9 p.m. to 1 a.m., which was pale. The patient weighed to-day 9 st. 5 lb.
	5 to 9 a.m.	1027	4	7·56	30			
	9 to 1 p.m.	1010	24	2·35	56			
	1 to 5 p.m.	1015	18¼	4·70	86			
	5 to 9 p.m.	1022	9	7·50	67			
	9 to 1 a.m.	1015	36	7·05	254			
Feb. 16	1 to 5 a.m.	1029	11½	12·97	149	1198	6 a.m., milk ½ pint 9 a.m., 1 chop 1 p.m., meat 8 oz., milk 1 pint 4 p.m., milk ½ pint 8 p.m., meat 8 oz., milk 1 pint	The specimens of urine from 1 to 5 a.m., 5 to 9 a.m., and 9 a.m. to 1 p.m., were pretty fairly coloured; that from 5 to 9 p.m. was pale.
	5 to 9 a.m.	1030	9	16·35	147			
	9 to 1 p.m.	1032	6½	15·63	102			
	1 to 5 p.m.	1030	14½	15·	217			
	5 to 9 p.m.	1012	38	7·65	291			
	9 to 1 a.m.	1020	26	11·25	292			

Feb. 17	1 to 5 a.m.	[illegible]	8	17·76	142	1258		The specimens of urine from 1 to 5 a.m., 5 to 9 a.m., and 9 a.m. to 1 p.m., were moderately high coloured; that from 5 to 9 p.m. was pale.
	5 to 9 a.m.	1040	7	21·18	150		6 a.m., 1 chop	
	9 to 1 p.m.	1030	5	14·82	74		1 p.m., meat 10 oz., milk 1 pint	
	1 to 5 p.m.	1020	21¼	8·31	177		4 p.m., meat 4 oz., milk 1 pint	
	5 to 9 p.m.	1015	37	9·84	364		8 p.m., meat 2 oz., milk 1 pint	
	9 to 1 a.m.	1023	20	17·55	351			
Feb. 18	1 to 5 a.m.	1030	9⅓	18·93	180	1485		The specimens of urine from 1 to 5 a.m., 5 to 9 a.m., and 9 a.m. to 1 p.m., were pretty fairly coloured; those from 1 to 5 p.m. and 9 p.m. to 1 a.m. were pale.
	5 to 9 a.m.	1037	8¼	23·58	195		6 a.m., 1 chop	
	9 to 1 p.m.	1020	11⅓	11·07	160		1 p.m., meat 10 oz., milk 1 pint	
	1 to 5 p.m.	1016	21¼	9·33	226		4 p.m., milk 1 pint, with suet ¼ lb.	
	5 to 9 p.m.	1031	9½	24·	228		8 p.m., meat 6 oz., milk 1 pint, with suet ¼ lb.	
	9 to 1 a.m.	1020	33⅓	14·82	496			
Feb. 19	1 to 5 a.m.	1030	8	20·55	164	1722	6 a.m., meat 8 oz.	The specimens of urine from 1 to 5 a.m., 5 to 9 a.m., and 9 a.m. to 1 p.m., were moderately high coloured; that from 9 p.m. to 1 a.m. was pale.
	5 to 9 a.m.	1035	7½	22·50	169		1 p.m., 1 chop, milk 1 pint, with suet ¼ lb.	
	9 to 1 p.m.	1038	9	24·81	223			
	1 to 5 p.m.	1032	11	21·81	240		4 p.m., milk 1 pint, with suet ¼ lb.	
	5 to 9 p.m.	1030	16	22·50	360		8 p.m.. 1 chop, milk 1 pint, with suet ¼ lb.	
	9 to 1 a.m.	1022	32¼	17·55	566			
Feb. 20	1 to 5 a.m.	1032	22	24·	528	2225		The specimens of urine from 5 to 9 a.m. and 9 a.m. to 1 p.m. were moderately high coloured; that from 9 p.m. to 1 a.m. was pale.
	5 to 9 a.m.	1040	7	22·50	157		6 a.m., 1 chop	
	9 to 1 p.m.	1037	10¼	24·	246		11 a.m., milk 1 pint, with suet ¼ lb.	
	1 to 5 p.m.	1035	11	25·71	283		1 p.m., meat 8 oz.	
	5 to 9 p.m.	1033	10¼	26·64	273		4 p.m., meat 4 oz., milk 1 pint	
	9 to 1 a.m.	1025	41	18·	738		8 p.m., meat 4 oz., milk 1 pint	
Feb. 21	1 to 5 a.m.	1037	9	26·64	240	927		The specimens of urine from 1 to 5 a.m., 5 to 9 a.m., and 9 a.m. to 1 p.m., were fairly coloured; that from 9 p.m. to 1 a.m. was of a pale yellow colour. The specimens belonging to the three latter periods of the day deposited crystals of lithic acid. Weight of patient 9 st. 5 lb.
	5 to 9 a.m.	1040	7¼	23·22	168		6 a.m., 4 eggs, hard boiled	
	9 to 1 p.m.	1035	8½	17·55	149		11 a.m., 2 eggs, hard boiled	
	1 to 5 p.m.	1032	7	10·74	75		1 p.m., meat 8 oz., beef tea 1 pint	
	5 to 9 p.m.	1033	5¾	12·63	73		4 p.m., meat 4 oz.	
	9 to 1 a.m.	1015	27½	8·07	222		8 p.m., meat 4 oz., beef tea 1 pint	
Feb. 22	1 to 5 a.m.	1027	8	12·51	100	734		The specimens of urine from 5 to 9 a.m., 1 to 5 p.m., and 5 to 9 p.m., were high coloured; that from 9 p.m. to 1 a.m. was pale. The specimen from 9 a.m. to 1 p.m. was milk white and opaque, from deposition of lithates. The specimens from 1 to 5 a.m. and 9 a.m. to 1 p.m. threw down crystals of lithic acid.
	5 to 9 a.m.	1028	14½	10·74	156		6 a.m., 4 eggs, hard boiled	
	9 to 1 p.m.	1027	5½	6·36	35		10.30 a m., 4 eggs, hard boiled	
	1 to 5 p.m.	1032	10	7·56	76		1 p.m., 1 chop, beef tea 1 pint	
	5 to 9 p.m.	1037	6½	15·63	102		8 p.m., 1 chop, beef tea 1 pint	
	9 to 1 a.m.	1020	27¼	9·72	265			

[1] These 2 pints of jelly were flavoured with 2 oz. of sugar, a little sherry and essence of lemon. [2] This jelly was without sugar, but with the sherry and essence of lemon.

Date	Period of day.	Sp gr. of urine.	Quantity of urine in oz.	Quantity of sugar per oz. of urine in grs.	Quantity of sugar in the urine per 4 hrs. in grs.	Quantity of sugar in the urine per 24 hrs. in grs.	Diet taken, with 4 oz. of brandy and 2 bottles of soda water daily, and 1 gr. of opium three times a day. Tea (without sugar), and water ad libitum.	REMARKS.
Feb. 23	1 to 5 a.m.	1030	21	17·55	369	1310	6 a.m., oysters 4 doz. 1 p.m., meat 16 oz., beef tea 1 pint 6 p.m., beef tea 1 piut 8 p.m., beef tea 1 pint	The specimens of urine from 1 to 5 a.m., 5 to 9 a.m., and 9 a.m. to 1 p.m., were pretty highly coloured; that from 9 p.m. to 1 a.m. was straw-coloured.
	5 to 9 a.m.	1030	14	16·92	237			
	9 to 1 p.m.	1027	14	14·67	205			
	1 to 5 p.m.	1030	15	6·54	98			
	5 to 9 p.m.	1017	13¾	11·07	152			
	9 to 1 a.m.	1012	38	6·54	249			
Feb. 24	1 to 5 a.m.	1020	28	10·56	296	896	7 a.m., oysters 4 doz. 1 p.m., meat 12 oz., beef tea 1 pint 4 p.m., meat 4 oz. 6.30 p.m., beef tea 1 pint 8 p.m., beef tea 1 pint	The specimen of urine from 5 to 9 a.m. was the highest coloured, and that from 9 a.m. to 1 p.m. the least so. The urine passed between 1 and 5 p.m. threw down a copious deposit of lithates.
	5 to 9 a.m.	1028	9	11·61	104			
	9 to 1 p.m.	1026	10	10·56	106			
	1 to 5 p.m.	1032	6½	2·4	16			
	5 to 9 p.m.	1025	10	6·15	61			
	9 to 1 a.m.	1015	33½	9·33	313			
Feb. 25	1 to 5 a.m.	1027	17½	15·	262	867	6 a.m., 1 chop 1 p.m., meat 4 oz., beef tea 1 pint 4 p.m., meat 4 oz. 6.30 p.m., beef tea 1 pint 8 p.m., beef tea 1 pint	The specimens of urine from 5 to 9 a.m. presented the highest colour; that from 9 p.m. to 1 a.m. was of a pale straw.
	5 to 9 a.m.	1034	5¼	12·63	73			
	9 to 1 p.m.	1028	9	10·26	92			
	1 to 5 p.m.	1031	13	12·18	158			
	5 to 9 p.m.	1030	9	12·84	116			
	9 to 1 a.m.	1015	24	6·90	166			
Feb. 26	1 to 5 a.m.	1022	27	12·	324	886	6 a.m., 1 chop 10.30, suet 4 oz. 1 p.m., 1 chop, beef tea 1 pint 4 p.m., suet 4 oz. 7 p.m., beef tea 1 pint 8 p.m., 1 chop, beef tea 1 pint	All the specimens of urine were of a fairish yellow colour, but that from 5 to 9 a.m. was the darkest, and that from 9 p.m. to 1 a.m. the palest.
	5 to 9 a.m.	1031	16	14·4	230			
	9 to 1 p.m.	1025	11	7·80	86			
	1 to 5 p.m.	1019	12	trace of sugar only				
	5 to 9 p.m.	1023	6	6·				
	9 to 1 a.m.	1015	31	6·78	210			
Feb. 27	1 to 5 a.m.	1026	16½	12·84	212	1177	6 a.m., 1 chop, gum 4 oz. dissolved in water and drank at intervals during the morning 1 p.m., meat 8 oz. 4 p.m., beef tea 1 pint 7 p.m., meat 8 oz., beef tea 1 pint	The specimen of urine from 1 to 5 a.m. was the highest coloured, that from 5 to 9 p.m. the least so. Weight of patient, 9 st. 10 lb.
	5 to 9 a.m.	1035	7	15·30	107			
	9 to 1 p.m.	1035	7	16·74	117			
	1 to 5 p.m.	1037	11¼	18·	202			
	5 to 9 p.m.	1023	33[illegible]	9·27	313			
	9 to 1 a.m.	1024	19½	11·61	226			

	1 to 5 a.m.	[illegible]	[illegible]	[illegible]	[illegible]		6 a.m., 1 chop	The specimens of urine from 1 to 5 a.m., 5
	5 to 9 a.m.	1037	3	20·55	62		1 p.m., meat 8 oz., beef tea 1 pint	to 9 a.m., and 9 a.m. to 1 p.m., presented
Feb. 28	9 to 1 p.m.	1037	$9\frac{1}{2}$	19·44	185	887	4 p.m., meat 4 oz.	the highest colour; that from 9 p.m. to 1
	1 to 5 p.m.	1037	8	12·63	101		7 p.m., meat 4 oz., beef tea 1 pint	a.m. was of a straw colour. The specimen
	5 to 9 p.m.	1021	12	8·31	100		8 p.m., beef tea 1 pint	passed between 1 and 5 p.m. threw down
	9 to 1 a.m.	1017	28	9·39	263			lithates.
	1 to 5 a.m.	1030	12	12·39	149			The specimen of urine from 1 to 5 a.m. was
	5 to 9 a.m.	1032	2	7·2	14		6 a.m., 1 chop	the highest, and that from 9 p.m. to 1 a.m.
March 1	9 to 1 p.m.	1025	$8\frac{1}{2}$	5·79	49	594	1 p.m., 1 chop, greens	the least coloured. The specimens from 5
	1 to 5 p.m.	1024	8	trace of sugar only			2 p.m., beef tea 1 pint	to 9 a.m., 9 a.m. to 1 p.m., 1 to 5 p.m.,
	5 to 9 p.m.	1032	9	13·08	118		8 p.m., 1 chop, beef tea 1 pint	and 5 to 9 p.m., deposited lithates.
	9 to 1 a.m.	1021	26	10·14	264			
							6 a.m., 1 chop, bran biscuit 3 oz.	
	1 to 5 a.m.	1032	19	15·99	304		10 a.m., bran biscuit $5\frac{1}{2}$ oz.	
	5 to 9 a.m.	1040	8	29·37	235		1 p.m., meat 8 oz., bran biscuit 3 oz.,	The specimens of urine from 1 to 5 a.m.,
March 2	9 to 1 p.m.	1039	14	31·29	438	2630	beef tea 1 pint	5 to 9 a.m., and 9 a.m. to 1 p.m., were
	1 to 5 p.m.	1040	$15\frac{1}{2}$	32·70	507		4 p.m., meat 4 oz., bran biscuit 3 oz.	highish coloured; that from 5 to 9 p.m.
	5 to 9 p.m.	1040	20	30·63	613		6 p.m., beef tea 1 pint	was of a straw colour.
	9 to 1 a.m.	1037	20	26·64	533		8 p.m., meat 4 oz., bran biscuit 3 oz., beef tea 1 pint	
	1 to 5 a.m.	1038	19	27·15	516		6 a.m., 1 chop, bran biscuit 3 oz.	
	5 to 9 a.m.	1041	9	28·80	259		10 a.m., bran biscuit 3 oz.	
March 3	9 to 1 p.m.	1042	$14\frac{3}{4}$	33·48	494	3291	1 p.m., meat 8 oz., bran biscuit 3 oz., beef tea 1 pint	The specimen of urine from 5 to 9 a.m. was
	1 to 5 p.m.	1043	18	36·	648		4 p.m., meat 4 oz., bran biscuit 3 oz.	the highest coloured, that from 9 p.m. to
	5 to 9 p.m.	1039	$25\frac{1}{2}$	32·70	834		7 p.m., beef tea 1 pint	1 a.m. the least coloured.
	9 to 1 a.m.	1030	24	22·50	540		8 p.m., meat 4 oz., beef tea 1 pint	
	1 to 5 a.m.	1037	$25\frac{1}{2}$	25·71	656		6 a.m., 1 chop, gluten bread 3 oz.	
	5 to 9 a.m.	1037	$9\frac{1}{4}$	28·23	261		10 a.m., gluten bread 2 oz.	
March 4	9 to 1 p.m.	1038	20	30·	600	4079	1 p.m., meat 8 oz., gluten bread 2 oz., beef tea 1 pint	The specimens of urine from 1 to 5 a.m.,
	1 to 5 p.m.	1035	$25\frac{1}{4}$	30·63	773		4 p.m., gluten bread 3 oz., beef tea 1 pint.	5 to 9 a.m., and 9 a.m. to 1 p.m., were
	5 to 9 p.m.	1031	28	27·69	775		8 p.m., meat 4 oz., gluten bread 2 oz., beef tea 1 pint	highish coloured; the others were pale.
	9 to 1 a.m.	1032	43	23·58	1014			
	1 to 5 a.m.	1035	23	25·71	591		6 a.m., 1 chop	
	5 to 9 a.m.	1037	17	25·71	437		10 a.m., meat 4 oz., gluten bread $2\frac{1}{2}$ oz.	The specimens of urine from 5 to 9 a.m.
March 5	9 to 1 p.m.	1040	$11\frac{1}{4}$	31·29	352	3228	1 p.m., 1 chop, gluten bread 3 oz., beef tea 1 pint	and 9 a.m. to 1 p.m. presented the most
	1 to 5 p.m.	1037	35	30·	1050			colour; that from 1 to 5 p.m. the least.
	5 to 9 p.m.	1036	$17\frac{1}{4}$	25·71	443		7 p.m., beef tea 1 pint	Weight of patient, 9 st. 10 lb.
	9 to 1 a.m.	1035	18	19·71	355		8 p.m., 1 chop, beef tea 1 pint	

Date.	Period of day.	Sp.gr. of urine.	Quantity of urine in oz.	Quantity of sugar per oz. of urine in grs.	Quantity of sugar in the urine per 4 hrs. in grs.	Quantity of sugar in the urine per 24 hrs. in grs.	Diet taken, with 4 oz. of brandy and 2 bottles of soda water daily, and 1 gr. of opium three times a day. Tea (without sugar), and water ad libitum.	REMARKS.
March 6	1 to 5 a.m.	1039	8	18·45	148	751	6 a.m., 1 chop 1 p.m., meat 8 oz., beef tea 1 pint 4 p.m., meat 4 oz., beef tea 1 pint 7.30 p.m., meat 4 oz., beef tea 1 pint	The specimen of urine from 1 to 5 a.m. was pretty highly coloured, those from 5 to 9 p.m. and 9 p.m. to 1 a.m. were the palest. The specimens from 5 to 9 a.m., 9 a.m. to 1 p.m., and 1 to 5 p.m., deposited lithates.
	5 to 9 a.m.	1037	6	15·	90			
	9 to 1 p.m.	1038	5¾	16·92	97			
	1 to 5 p.m.	1040	7½	11·70	88			
	5 to 9 p.m.	1035	6½	14·25	93			
	9 to 1 a.m.	1029	19	12·39	235			
March 7	1 to 5 a.m.	1035	18¾	15·63	293	1188	6 a.m., 1 chop 1 p.m., meat 10 oz., beef tea 1 pint 4 p.m., beef tea 1 pint 7 p.m., meat 6 oz., beef tea 1 pint	The specimens of urine from 1 to 5 a.m., 5 to 9 a.m., and 9 a.m. to 1 p.m., were highish coloured; that from 9 p.m. to 1 a.m. was straw coloured.
	5 to 9 a.m.	1037	10¾	18·93	203			
	9 to 1 p.m.	1035	7	14·52	102			
	1 to 5 p.m.	1040	10½	18·45	194			
	5 to 9 p.m.	1033	14½	13·83	201			
	9 to 1 a.m.	1021	20¾	9·39	195			
March 8	1 to 5 a.m.	1032	16	12·96	207	3443	6 a.m., 1 chop, gluten bread 3 oz. 10.30 a.m., gluten bread 3½ oz. 1 p.m., 1 chop, gluten bread 3½ oz., beef tea 1 pint 4 p.m., gluten bread 2½ oz., beef tea 1 pint 8 p.m., 1 chop, gluten bread 1½ oz., beef tea 1 pint	The specimen of urine from 5 to 9 a.m. was highish coloured; the others were pale.
	5 to 9 a.m.	1036	13	28·23	367			
	9 to 1 p.m.	1037	15	31·29	469			
	1 to 5 p.m.	1037	28	30·	840			
	5 to 9 p.m.	1035	33	27·69	914			
	9 to 1 a.m.	1034	24¼	26·64	646			
March 9	1 to 5 a.m.	1034	33½	25·71	861	4539	6 a.m., 1 chop, gluten bread 2½ oz. 11 a.m., gluten bread 3 oz. 1 p.m., meat 8 oz., gluten bread 3 oz., beef tea 1 pint 4 p.m., gluten bread 3 oz., beef tea 1 pint 8 p.m., meat 8 oz., gluten bread 2½ oz., beef tea 1 pint	All the specimens of urine were of a straw colour, with scarcely any shade of difference between them.
	5 to 9 a.m.	1037	28	27·15	760			
	9 to 1 p.m.	1035	28	25·71	720			
	1 to 5 p.m.	1041	24	30·63	735			
	5 to 9 p.m.	1039	35	25·71	900			
	9 to 1 a.m.	1034	24¼	23·22	563			
March 10	1 to 5 a.m.	1035	28¼	24·81	701	1726	6 a.m., 1 chop 1 p.m., meat 8 oz., beef tea 1 pint 4 p.m., meat 4 oz., beef tea 1 pint 8 p.m., meat 4 oz., beef tea 1 pint	The specimens of urine from 1 to 5 a.m. and 9 a.m. to 1 p.m. were highish coloured; that from 9 p.m. to 1 a.m. was pale. The urine passed between 5 and 9 a.m. deposited lithates.
	5 to 9 a.m.	1040	4	19·20	77			
	9 to 1 p.m.	1035	10	16·35	163			
	1 to 5 p.m.	1039	11¼	19·44	219			
	5 to 9 p.m.	1032	15¾	15·99	252			
	9 to 1 a.m.	1031	19	16·53	314			

March 11	5 to 9 a.m.	1037	6	13·83	83	994	6 a.m., 1 chop	The specimen of urine from 1 to 5 a.m. was highish coloured, that from 5 to 9 p.m. pale. The urine voided between 5 and 9 a.m., 9 a.m. and 1 p.m., and 1 and 5 p.m., threw down lithates.
	9 to 1 p.m.	1032	7½	9·60	72		1 p.m., meat 8 oz., beef tea 1 pint	
	1 to 5 p.m.	1037	12½	10·56	132		4 p.m., meat 8 oz., beef tea 1 pint	
	5 to 9 p.m.	1020	29	9·72	282		7 p.m., beef tea 1 pint	
	9 to 1 a.m.	1025	21	12·30	258			
March 12	1 to 5 a.m.	1032	6	13·56	81	2587	6 a.m., half of a rice pudding composed of 4 oz. of rice and 1 egg	The specimen of urine from 1 to 5 a.m. was the highest coloured, that from 9 p.m. to 1 a.m. the least coloured.
	5 to 9 a.m.	1033	20	28·80	576		10 a.m., remainder of the rice pudding	
	9 to 1 p.m.	1035	26¾	31·29	837		1 p.m., 1 chop, beef tea 1 pint	
	1 to 5 p.m.	1042	12	31·29	375		4 p.m., beef tea 1 pint	
	5 to 9 p.m.	1039	15	22·50	337		8 p.m., 1 chop, beef tea 1 pint	
	9 to 1 a.m.	1025	27¼	13·98	381			
March 13	1 to 5 a.m.	1035	15¼	18·45	281	2270	6 a.m., potatoes 1 lb. (boiled)	The specimen of urine from 1 to 5 a.m. was highish coloured, that from 5 to 9 p.m. was of a palish straw and deposited lithates. Weight of patient, 9 st. 13 lb.
	5 to 9 a.m.	1032	32	24·81	794		11 a.m., 1 chop	
	9 to 1 p.m.	1040	16	31·29	501		1 p.m., meat 8 oz., beef tea 1 pint	
	1 to 5 p.m.	1044	7½	28·80	216		4 p.m., meat 4 oz., beef tea 1 pint	
	5 to 9 p.m.	1037	11½	16·35	188		8 p.m., meat 4 oz., beef tea 1 pint	
	9 to 1 a.m.	1026	20	14·52	290			
March 14	1 to 5 a.m.	1037	12	18·21	219	2278	6 a.m., arrowroot 1 oz. in 1 pint water	The specimen of urine from 1 to 5 a.m. was high coloured, that from 9 p.m. to 1 a.m. was pale.
	5 to 9 a.m.	1038	12	30·	360		9 a.m., arrowroot 1 oz. in 1 pint water	
	9 to 1 p.m.	1037	14	32·70	458		11 a.m., 1 chop	
	1 to 5 p.m.	1041	21	25·71	540		1 p.m., meat 12 oz., beef tea 1 pint	
	5 to 9 p.m.	1035	15	24·81	372		4 p.m., meat 4 oz., beef tea 1 pint	
	9 to 1 a.m.	1021	27	12·18	329		7 p.m., beef tea 1 pint	
March 15	1 to 5 a.m.	1030	16¾	11·79	197	3521	6 a.m., 1 chop, bread 4 oz.	The specimens of urine from 1 to 5 a.m. and 5 to 9 a.m. were of a highish colour, those from 1 to 5 p.m. and 9 p.m. to 1 a.m. were pale.
	5 to 9 a.m.	1032	14¼	27·15	387		1 p.m., 1 chop, beef tea 1 pint	
	9 to 1 p.m.	1034	25	31·98	800		4 p.m., beef tea 1 pint	
	1 to 5 p.m.	1037	22½	35·10	790		7.30 p.m., 1 chop, beef tea 1 pint	
	5 to 9 p.m.	1034	23½	30·	705			
	9 to 1 a.m.	1033	29	22·14	642			
March 16	1 to 5 a.m.	1040	15	22·50	337	2371	6 a.m., carrots 1 lb. (boiled)	The specimen of urine from 1 to 5 a.m. was highish coloured, those from 1 to 5 p.m., 5 to 9 p.m., and 9 p.m. to 1 a.m., were pale.
	5 to 9 a.m.	1038	12	28·80	346		9 a.m., carrots 1 lb. (boiled)	
	9 to 1 p.m.	1037	8	24·81	198		11 a.m., 1 chop	
	1 to 5 p.m.	1037	16	27·69	443		1 p.m., meat 12 oz., beef tea 1 pint	
	5 to 9 p.m.	1036	12	31·29	375		4 p.m., meat 4 oz., beef tea 1 pint	
	9 to 1 a.m.	1031	28	24·	672		8 p.m., beef tea 1 pint	

Date.	Period of day.	Sp.gr. of urine.	Quantity of urine. in oz.	Quantity of sugar per oz. of urine in grs.	Quantity of sugar in the urine per 4 hrs. in grs.	Quantity of sugar in the urine per 24 hrs. in grs.	Diet taken, with 4 oz. of brandy and 2 bottles of soda water daily, and 1 gr. of opium three times a day. Tea (without sugar), and water ad libitum.	REMARKS.
March 17	1 to 5 a.m.	1033	17¼	23·58	407	8319	6 a.m., bread 8 oz., butter ½ oz. 10 a.m., bread 5 oz., milk ½ pint 1 p.m., meat 5 oz., greens 3 p.m., suet pudding composed of suet, 1 egg, and a little flour; 2 oranges 4 p.m., tea with ½ pint milk and sugar 6 p.m., meat 4 oz., bread 4 oz., butter ½ oz. 7 p.m., 1 orange	The specimen of urine from 1 to 5 a.m. was pretty highly coloured, and next to it was that from 5 to 9 a.m. All the remaining specimens were exceedingly pale.
	5 to 9 a.m.	1032	26½	30·	795			
	9 to 1 p.m.	1030	60	30·	1800			
	1 to 5 p.m.	1039	38	37·89	1440			
	5 to 9 p.m.	1032	51	31·29	1596			
	9 to 1 a.m.	1032	65	35·10	2281			
March 18	1 to 5 a.m.	1040	32	36·	1152	8959	6 a.m., meat 4 oz., bread 4 oz., butter ½ oz., tea with sugar 10 a.m., meat 4 oz., bread 5 oz., 1 orange 11 a.m., milk 1 pint 1 p.m., meat 4 oz., greens 6 oz. 3 p.m. 1 orange 4 p.m., bread 5 oz., butter ½ oz., tea with sugar 7 p.m., 1 orange	All the specimens of urine were exceedingly pale in colour.
	5 to 9 a.m.	1038	30	36·	1080			
	9 to 1 p.m.	1035	65	34·26	2227			
	1 to 5 p.m.	1037	54	34·75	1876			
	5 to 9 p.m.	1034	29	35·80	1038			
	9 to 1 a.m.	1035	45	35·25	1586			
March 19	1 to 5 a.m.	1040	31	33·30	1032	8355	6 a.m., bread 4 oz., butter ½ oz., 1 pint cocoa with sugar 11·30 a.m., bread 5 oz., butter ¼ oz., milk ½ pint 1 p.m., soup 1 pint (meat and vegetable), bread 3 oz. 2 p.m. milk ½ pint 3 p.m., 1 orange 4 p.m., bread 4 oz., butter ¼ oz., tea with sugar	All the specimens of urine were exceedingly pale coloured, but that from 1 to 5 a.m. was the highest. Weight of patient, 9 st. 12 lb.
	5 to 9 a.m.	1042	28¼	36·90	1042			
	9 to 1 p.m.	1039	31	36·35	1127			
	1 to 5 p.m.	1039	57	36·35	2072			
	5 to 9 p.m.	1032	46	34·25	1575			
	9 to 1 a.m.	1031	49	30·75	1507			
March 20	1 to 5 a.m.	1041	44	39·30	1729	8965	6 a.m., bread 4 oz., butter ½ oz., tea with sugar 10 a.m., bread 4 oz., meat 3 oz., milk ½ pt. 1 p.m., meat 4 oz., greens, milk ½ pint 2 p.m., 1 orange 4 p.m., bread 4 oz., butter ½ oz., tea with sugar 7 p.m., 1 orange	All the specimens of urine were exceedingly pale coloured.
	5 to 9 a.m.	1039	31	39·30	1218			
	9 to 1 p.m.	1038	39	37·50	1462			
	1 to 5 p.m.	1040	43	34·25	1473			
	5 to 9 p.m.	1036	49	34·75	1703			
	9 to 1 a.m.	1038	41	33·65	1380			

	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]			
March 21	5 to 9 a.m.	1018	7	30·	210	1962	6 a.m. 1 chop	The specimens of urine from 1 to 5 a.m. and 5 to 9 a.m. were moderately coloured, the other specimens were pale.
	9 to 1 p.m.	1045	6	19·71	118		1 p.m., meat 8 oz., beef tea 1 pint	
	1 to 5 p.m.	1015	10	23·22	232		4 p.m., meat 4 oz., beef tea 1 pint	
	5 to 9 p.m.	1037	17	23·58	401		8 p.m., meat 4 oz., beef tea 1 pint	
	9 to 1 a.m.	1026	22	13·83	304			
March 22	1 to 5 a.m.	1036	10	15·81	158	1330		The specimen of urine from 1 to 5 a.m. was pretty highly coloured, that from 9 p.m. to 1 a.m. was pale. The urine passed between 9 a.m. and 1 p.m. threw down a copious deposit of lithates.
	5 to 9 a.m.	1037	7	18·	126		6 a.m., 1 chop	
	9 to 1 p.m.	1035	6	11·25	67		1 p.m., 1 chop, beef tea 1 pint	
	1 to 5 p.m.	1035	15	17·76	266		4 p.m., beef tea 1 pint	
	5 to 9 p.m.	1027	18	19·44	350		8 p.m., 1 chop, beef tea 1 pint	
	9 to 1 a.m.	1023	28	12·96	363			
March 23	1 to 5 a.m.	1032	24	18·	432	2113	6 a.m., 1 chop	The specimen of urine passed between 5 and 9 a.m. was the highest coloured.
	5 to 9 a.m.	1033	8	17·76	142		1 p.m., meat 8 oz.	
	9 to 1 p.m.	1037	12	22·50	270		2 p.m., beef tea 1 pint	
	1 to 5 p.m.	1038	16¼	26·16	425		4 p.m., beef tea 1 pint	
	5 to 9 p.m.	1035	12	20·28	243		8 p.m., meat 8 oz., beef tea 1 pint	
	9 to 1 a.m.	1034	25½	23·58	601			

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